Express Mail Label No. EM601204925US

UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	FJN-060DV2 (3999/63)
First Named Inventor	Goto et al.
Title	NOVEL PROTEINS AND METHODS FOR PRODUCING THE PROTEINS

APPLICATION ELEMENTS	ADDRESS TO: **Box Patent Application, Assistant Commissioner for Patents, Washington, D.C. 20231**
1. ☒ Fee Transmittal Form	**ACCOMPANYING APPLICATION PARTS**
2. ☒ Specification and Drawings [Total Pages 181] - Specification - (165 pages) - Claims - (4 pages) - Abstract - (1 page) - Sheets of Drawings - (11 sheets) ☐ Formal ☒ Informal	7. ☐ 37 CFR 3.73(b) Statement (when there is an assignee) ☐ Power of Attorney
	8. ☐ English Translation Document *(if applicable)*
	9. ☒ Information Disclosure Statement (IDS)/PTO-1449 ☒ Copies of IDS Citations
3. ☒ Oath or Declaration [Total Pages 6] a. ☐ Newly executed (original) b. ☒ Copy from a prior application (37 CFR 1.63(d)) *(for continuation/divisional with Box 17 completed)* ***[Note Box 4 below]***	10. ☒ Preliminary Amendment ☐ Drawings [Total Sheets] ☐ Letter to Official Draftsperson Including Drawings [Total Pages]
	11. ☒ Return Receipt Postcard
4. ☒ Incorporation by Reference (usable if Box 3b is checked) The entire Disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 3b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.	12. ☐ Small Entity Statement(s) ☐ Statements filed in prior application, (Status still proper and desired)
	13. ☐ Certified Copy of Priority Document(s)
5. ☐ Microfiche Computer Program *(Appendix)*	14. ☐ Deletion of Inventor(s) Signed statement attached deleting inventor(s) named in the prior application.
6. ☒ Nucleotide and/or Amino Acid Sequence Submission ☐ Computer Readable Copy ☒ Paper Copy (identical to computer copy) ☐ Statement verifying identify of above copies	15. ☒ Patent Application Data Entry Form
	16. ☒ Other: Associate Power of Attorney

17. ☒ **If a CONTINUING APPLICATION,** check appropriate box and supply the requisite information:
☐ Continuation ☒ Divisional ☐ Continuation-in-part (CIP) of prior application Serial No. 08/915,004.
Priority to the above application(s) is claimed under 35 U.S.C. 120.
Prior application information: Examiner: Degen. Group/Art Unit: 1636.

18. ☒ **Priority - 35 U.S.C. 119**
☒ Priority of application Serial No. JP 54977, filed on February 20, 1995 and JP 207508/1995 filed on July 21, 1995 in Japan is claimed under 35 U.S.C. 119.
☒ The certified copy has been filed in prior U.S. application Serial No. 08/915,004 on October 14, 1998.
☐ The certified copy will follow.

CORRESPONDENCE ADDRESS	SIGNATURE BLOCK
Direct all correspondence to: Patent Administrator Testa, Hurwitz & Thibeault, LLP High Street Tower 125 High Street Boston, MA 02110 Tel. No.: (617) 248-7000 Fax No.: (617) 248-7100	Date: June 23, 1999 Reg. No. 44,244 Tel. No.: (617) 248-7044 Fax No.: (617) 248-7100 Respectfully submitted, Ronda P. Moore, D.V.M. Attorney for Applicants Testa, Hurwitz & Thibeault, LLP High Street Tower 125 High Street Boston, MA 02110

Rmoore3999/63.807653-1

Express Mail Label No. EM601204925US

FEE TRANSMITTAL

Note: Effective October 1, 1997.
Patent fees are subject to annual revision

Complete if Known	
Application Serial Number	Not yet assigned
Filing Date	Herewith
First Named Inventor	Goto et al.
Group Art Unit	Not yet assigned
Examiner Name	Not yet assigned
Attorney Docket No.	FJN-060DV2 (3999/63)

METHOD OF PAYMENT

1. ☒ Payment Enclosed:
   ☒ Check ☐ Money Order ☐ Other

2. ☒ The Commissioner is hereby authorized to credit or charge any fee indicated below to Deposit Account No. 20-0531.
   ☐ Required Fees (copy of this sheet enclosed).
   ☒ Additional fee required under 37 CFR 1.16 and 1.17.
   ☒ Overpayment Credit.

FEE CALCULATION

1. FILING FEE

Large Entity Fee ($)	Fee Description	Fee Paid
760	Utility filing fee	760.00
310	Design filing fee	
150	Provisional filing fee	

	Number Filed	Number Extra	Rate	Amount
Total Claims	5	- 20 = 0	x $ 18.00 =	0
Independent Claims	2	- 3 = 0	x $ 78.00 =	0
☐ Multiple Dependent Claim(s), if any			$260.00 =	

TOTAL: 760.00
SMALL ENTITY DISCOUNT: 0
SUBTOTAL (1) ($) 760.00

2. AMENDMENT CLAIM FEES

Claims Remaining After Amend.	Highest No. Previously Paid For	Present Extra	Rate	Fee Paid
Total	-	=	x $ 18.00 =	
Indep.	-	=	x $ 78.00 =	
☐ First Presentation of Multiple Dep. Claim			+ $260.00 =	

TOTAL: ($)
SMALL ENTITY DISCOUNT: ($)
SUBTOTAL (2) ($) 0

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee ($)	Small Entity Fee ($)	Fee Description	Fee Paid
130	65	Surcharge - late filing fee or oath	
50	25	Surcharge - late provisional filing fee or	
130	130	Non-English specification	
2,520	2,520	For filing a request for reexamination	
110	55	Extension for reply within first month	
380	190	Extension for reply within second month	
870	435	Extension for reply within third month	
1,360	680	Extension for reply within fourth month	
1,850	925	Extension for reply within fifth month	
300	150	Notice of Appeal	
300	150	Filing a brief in support of an appeal	
260	130	Request for oral hearing	
130	130	Petitions to the Commissioner	
50	50	Petitions related to provisional applications	
240	240	Submission of Information Disclosure Statement (37 CFR 1.97(c))	
130	130	Submission of Information Disclosure Statement (37 CFR 1.97(d))	
760	380	Filing a submission after final rejection (37 CFR 1.129(a))	
760	380	For each additional invention to be examined (37 CFR 1.129(b))	
		Other (Specify)	

SUBTOTAL (3) ($)

SUBTOTAL (1)	760.00
SUBTOTAL (2)	0
SUBTOTAL (3)	0
TOTAL	($) 760.00

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Rmoore3999/63.807682-1

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Date: June 23, 1999
Reg. No.: 44,244
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State/Prov. of Residence ::
Country of Residence :: Japan
Citizenship :: Japan

Correspondence Information

Correspondence Customer Number :: 021323

Application Information

Title Line One :: NOVEL PROTEINS AND METHODS FOR
Title Line Two :: PRODUCING THE PROTEINS
Total Drawing Sheets :: 11
Formal Drawings ::
Application Type :: Divisional
Docket Number :: FJN-060DV2
Licensed - U S Government Agency ::
Contract Number ::
Grant Number ::
Secrecy Order in Parent Application ::

Representative Information

Representative Customer Number :: 021323

Continuity Information

This application is a :	Divisional
>Application One ::	08/915,004
Filing Date ::	October 14, 1998
Patent Number ::	
which is a ::	
>>Application Two ::	
Filing Date ::	
Patent Number ::	

Prior Foreign Applications

Foreign Application One ::	JP 54977
Filing Date ::	February 20, 1995
Country ::	Japan
Priority Claimed ::	Yes

Foreign Application Two::	JP 207508/1995
Filing Date::	July 21, 1995
Country::	Japan
Priority Claimed::	Yes

Rmoore3999/63.809464-1

EXPRESS MAIL MAILING LABEL
No. EM601204925US

PATENT
FJN-060DV2
(3999/63)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT
Attorney Docket No. FJN-060DV2
(3999/63)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S):	Goto et al.		
SERIAL NO.:	Not yet assigned	GROUP NO.:	Not yet assigned
FILING DATE:	Herewith	EXAMINER:	Not yet assigned
TITLE:	NOVEL PROTEINS AND METHODS FOR PRODUCING THE PROTEINS		

Box Patent Application
Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Please amend the above-identified divisional patent application as follows:

IN THE ABSTRACT:

Please delete the Abstract and insert the following:

--An antibody having special affinity to a protein which inhibits osteoclast differentiation and/or maturation and a method for determining the concentration of the protein by detection of the concentration of protein-antibody conjugates formed. The protein is produced by human embryonic lung fibroblasts and has a molecular weight of about 60 kD and about 120 kD under non-reducing conditions and about 60 kD under reducing conditions on SDS-polyacrylamide gel

electrophoresis. The protein can be isolated and purified from the culture medium of fibroblasts. Furthermore, the protein can be produced by gene engineering.--

IN THE SPECIFICATION:

Applicants have amended the specification to correct translation errors and to claim benefit of an earlier filing date. No new matter is being introduced. Please enter the following amendments:

Page 1, After the title "Novel Proteins and Methods for Producing the Proteins" and before "Field of the Invention," insert --This is a divisional application of U.S.S.N. 08/915,004, filed on August 20, 1997, which was a continuation-in-part of PCT/JP96/00374, filed on February 20, 1996, and which designated the U.S. and claims priority to JP54977/1995, filed on February 20, 1995, and JP207508/1995, filed on July 21, 1995.--

Line 8, delete "In the process, osteoblasts" and insert --Osteoblasts--;

Line 10, after "of" (first occurrence) insert --a--; delete "the progression of";

Line 11, delete "The disease" and insert --Osteoporosis--; delete "be provoked" and insert --result--;

Line 12, delete "by the condition in which" and insert --when--;

Line 14, after "causes" insert --bone--; delete "in the bone"; after "makes" delete "the bone" and insert --bone's--;

Line 15, delete the line in its entirety and insert --fragile, leading to fracture, particularly in elderly patients.--;

Line 16, delete "bedridden old people, it has" and insert --Osteoporosis has therefore--;

Line 17, delete "old" and insert --elderly--; after "people" insert --in the population--; delete "efficacious" and insert --effective--;

Line 18, delete "the";

Line 20, delete "balanced" and insert --balance of bone--;

Line 21, delete "expected to be";

Line 22, delete "are reported" and insert --reportedly--; and

Line 23, delete "to".

Page 2, Line 4, delete "Mol" and insert --Mol.--;

Line 5, after "M" insert a period --.--;

Line 7, after "A" insert a period --.--;

Line 9, delete "1993" and insert --1993)--;

Line 10, delete "inhibits" and insert --inhibit--;

Line 11, delete "have been paid attention and have"; and insert --have also--;

Line 14, delete "are found to";

Line 15, delete "Macrophage" and insert --macrophage--;

Line 19, delete "are found";

Line 21, delete "efficacious" and insert --effective--;

Line 23, delete "The cytokines" and insert --Cytokines--; delete "insulin like" and insert --insulin-like--; and

Line 24, delete "are now" and insert --have been--;

Page 3, Line 1, delete "effects in treatment of" and insert --effectiveness for treating--;

Line 2, delete "as a drug to care" and insert --to treat--; after "osteoporosis" (second occurrence) insert --patients--;

Line 6, delete "preparations ." and insert --preparations.--;

Line 7, delete "have been" and insert --are--;

Line 8, delete "As mentioned," and insert --Since--; delete "controlled" and insert --manifest--;

Line 9, delete ". Therefore";

Line 12, delete "Disclosure" and insert --Summary--;

Line 13, delete the line in its entirety and insert --The--;

Line 14, after "factor" insert a comma --,--;

Line 15, after "(OCIF)" insert a comma --,--;

Line 22, delete "using" and insert --on--; after "pieces" insert --, which function--; and

Line 23, delete "the".

Page 4, Line 3, delete "chromatography," and insert --chromatography:--;

Line 5, delete "The inventors, based on" and insert --After determining--;

Line 6, delete the line in its entirety and insert --OCIF, a cDNA encoding this protein was successfully cloned.--;

Line 7, delete the line in its entirety and insert --A procedure for producing this protein was also established--;

Line 8, delete "differentiation of osteoclasts. This" and insert --The--;

Line 9, after "has" insert --a--; delete "weights in" and insert --weight by--;

Line 10, delete "in the" and insert --under--; before "non-reducing" delete "the"; after "conditions," (second occurrence) and insert --and--;

Line 11, delete "heparin, reduces its activity" and insert --heparin.--;

Line 12, before "to" insert --The protein's ability--; after "inhibit" insert --the--; delete "if" and insert --is reduced when--;

Line13, delete "lose its activity" and insert --its ability--;

Line 14, delete "by the treatment" and insert --is lost when treated--;

Line 15, delete "protein OCIF which is described in" and insert --OCIF protein of--;

Line 16, delete "of know factors inhibiting" and insert --other factors known to inhibit the--;

Line 18, delete "to purify" and insert --for purifying--; delete "comprising ;" and insert --comprising:--;

Line 23, before "(6)" insert --and--; and

Line 24, after "F3GA" insert --may be--.

Page 5, Line 1, delete the line in its entirety and insert --hydrophilic polymers, for example.--;

Line 2, delete "columns." (first occurrence); delete "colomns" and insert --columns--;

Line 3, delete "accumulating the" and insert --producing--; delete "to a" and insert --in--;

Line 6, delete "the" (third occurrence);

Line 7, after "the" insert --oligonucleotide--;

Before Line 10 insert

--Brief Description of the Figures

Figure 1 shows the elution pattern of crude OCIF protein (Hiload-Q/FF pass-through fraction; sample 3) from a Hiload-S/HP column.

Figure 2 shows the elution pattern of crude OCIF protein (heparin-5PW fraction; sample 5) from a blue-5PW column.

Figure 3 shows the elution pattern of OCIF protein (blue-5PW fraction 49 to 50) from a reverse-phase column.

Figures 4A and 4B shows the SDS-PAGE of isolated OCIF proteins under reducing or non-reducing conditions. Description of the lanes:

lane 1, 4: molecular weight marker proteins;

lane 2, 5: OCIF protein of peak 6 in figure 3;

lane 3, 6: OCIF protein of peak 7 in figure 3.

Figure 5 shows the elution pattern of peptides obtained by the digestion of pyridyl ethylated OCIF protein digested with lysylendopeptidase, on a reverse-phase column.

Figure 6 shows the SDS-PAGE of isolated natural (n) OCIF protein and recombinant (r) OCIF proteins under non-reducing conditions. rOCIF (E) and rOCIF (C) proteins were produced in 293/EBNA cells and in CHO cells, respectively. Description of the lanes:

lane 1: molecular weight marker proteins;

lane 2: a monomer type nOCIF protein;

lane 3: a dimer type nOCIF protein;

lane 4: a monomer type rOCIF (E) protein;

lane 5: a dimer type rOCIF (E) protein;

lane 6: a monomer type rOCIF (C) protein;

lane 7: a dimer type rOCIF (C) protein.

Figure 7 shows the SDS-PAGE of isolate natural (n) OCIF proteins and recombinant (r) OCIF proteins under reducing conditions. rOCIF (E) and rOCIF (C) were produced in 293 EBNA cells and in CHO cells, respectively. Description of the lanes:

lane 8: molecular weight marker proteins;

lane 9: a monomer type nOCIF protein;

lane 10: a dimer type nOCIF protein;

lane 11: a monomer type rOCIF (E) protein;

lane 12: a dimer type rOCIF (E) protein;

lane 13: a monomer type rOCIF (C) protein;

lane 14: a dimer type rOCIF (C) protein.

Figure 8 shows the SDS-PAGE of isolated natural (n) OCIF proteins and recombinant (r) OCIF proteins from which N-linked sugar chains were removed under reducing conditions. rOCIF (E) and rOCIF (C) are rOCIF proteins produced in 293/EBNA cells and in CHO cells, respectively. Description of the lanes:

lane 15: molecular weight marker proteins;

lane 16: a monomer type nOCIF protein;

lane 17: a dimer type nOCIF protein;

lane 18: a monomer type rOCIF (E) protein;

lane 19: a dimer type rOCIF (E) protein;

lane 20: a monomer type rOCIF(C) protein;

lane 21: a dimer type rOCIF(C) protein.

Figure 9 shows a comparison of OCIF and OCIF2 amino acid sequences.

Figure 10 shows a comparison of OCIF and OCIF3 amino acid sequences.

Figure 11 shows a comparison of OCIF and OCIF4 amino acid sequences.

Figure 12 shows a comparison of OCIF and OCIF5 amino acid sequences.

Figure 13 shows a standard curve determining OCIF protein concentration by an EIA employing anti-OCIF polyclonal antibodies.

Figure 14 shows a standard curve determining OCIF protein concentration by an EIA employing anti-OCIF monoclonal antibodies.

Figure 15 shows the effect of rOCIF protein on osteoporosis.--;

Page 5, Line 15, delete "procedure includes" and insert --procedures include--;

Line 16, delete "lyophylization" and insert --lyophilization--; delete "procedure includes" and insert --procedures include--;

Line 21, delete the line in its entirety and insert --fibroblasts used for the production of OCIF protein are preferably IMR-90 cells. A--; and

Line 22, delete "the".

Page 6, Line 1, delete ", using" and insert --in--;

Line 2, delete "for the cell culture";

Line 4, delete "prefarably" and insert --preferably--;

Line 5, before "purification steps of OCIF protein." and insert --protein purification procedure.--

Line 6, before "OCIF" insert --The--; delete "initially obtained" and insert --obtained initially--;

Line 7, delete "heparin binding basic" and insert --basic heparin binding--; delete "basic";

Line 9, delete "then by";

Line 10, before "non-" insert --the--;

Line 13, delete the period "." and insert a comma --,--; before "Cibacrone" insert --a--;

Line 14, delete "Elmer) and" and insert --Elmer).--;

Line 15, delete the line in its entirety.

Line 17, delete "method of" and insert --method for--;

Line 18, delete "protein that inhibits differentiation and/or" and insert --protein.--; and

Line 19, delete "maturation of osteoclasts.".

Page 7, Line 1, delete "was systhesized." and insert --is synthesized.--;

Line 4, delete "the" (second occurrence);

Line 5, delete "obtained" and insert --an--;

Line 6, delete "The recombinant" and insert --Recombinant--;

Line 7, after "cDNA" insert a comma --,--; after "region" insert a comma --,--;

Line 12, delete "by hybridization" and insert --and--; before "probe" insert --hybridization--;

Line 14, before "can be" insert --protein--;

Line 15, after "cDNAs" insert a comma --,--; after "region" insert a comma --,--;

Line 16, after "in" delete "the"; after "variant" insert --protein--;

Line 18, after "variant" insert --protein--; delete "an" and insert --the--;

Line 20, before "replacement" insert --the--; after "residue" insert a comma --,--; and

Line 21, delete "formation with serine residue, and" and insert --formation, with a serine residue or--.

Page 8, Line 1, delete "by";

Line 2, delete "containing" and insert --having--;

Line 9, delete "As antigens (immunogens), natural" and insert --Natural--;

Line 11, delete "designed";

Line 13, delete "used." and insert --used as antigens.--;

Line 14, after "antigens" insert a comma --,--; delete "for immunization";

Line 15, delete "purifying from the serum by the" and insert --and purifying the antibodies from the serum by--; delete "The";

Line 16, delete "anti-OCIF" and insert --Anti-OCIF--; delete "rasioisotopes" and insert --radioisotopes--;

Line 17, delete "system or immunoassay (EIA) system." and insert --systems or enzyme-immunoassay (EIA) systems.--;

Line 18, delete "By using" and insert --Using--; delete "concentrations" and insert --concentration--;

Line 19, delete "blood and" and insert --blood,--; delete "cells-culture" and insert --cell-culture--;

Line 21, delete the line in its entirety;

Line 22, delete the line in its entirety; and

Line 23, delete the line in its entirety.

Page 9, Line 1, delete the line in its entirety;

Line 3, delete "to" and insert --for--; delete "determine" and insert --determining--;

Line 5, delete "the";

Line 6, delete "method" and insert --methods--;

Line 8, delete "using" and insert --transfected with--;

Line 9, delete "synthesized peptides designed" and insert --synthetic peptides--;

Line 11, delete "immunization of mammals" and insert --immunizing mammals such as mice or rats--;

Line 12, delete "mycloma of mammals" and insert --mammalian myeloma cells--;

Line 13, delete "hybridoma." and insert --hybridomas.--; delete "antibody" and insert --antibodies--; delete "recognizes" and insert --recognize--;

Line 14, delete the line in its entirety and insert --OCIF were selected and cultured to obtain the desired antibodies.--;

Line 15, delete the line in its entirety;

Line 16, delete the line in its entirety;

Line 17, delete the line in its entirety and insert --For immunizations, OCIF is suitably diluted with--;

Line 19, delete "for";

Line 20, after "after" insert --the--;

Line 21, delete "was taken out" and insert --removed--; delete "were"; and

Line 22, after "lines" insert --useful--; delete "the".

Page 10, Line 1, delete the line in its entirety and insert --Ag8.653, and S194 cells. The rat cell line R-210 may also be used. Alternatively, human B lymphocytes--;

Line 2, before "immunized" delete "are"; delete "and";

Line 3, delete "cell line" and insert --cells--; delete "which are used";

Line 4, delete the line in its entire and insert --to produce human type antibodies.--;

Line 5, delete "the"; delete "cell line" and insert --cells--;

Line 6, after "by" delete "the";

Line 7, delete "used, and also" and insert --used. Alternatively--;

Line 8, delete "applied to cell fusion." and insert --used.--;

Line 11, delete the line in its entirety and insert --used to fuse the cells. The fusion products are--;

Line 12, delete "hybridoma." and insert --for hybridomas.--;

Line 13, delete the line in its entirety and insert --An EIA, plaque--;

Line 14, delete "principally used. Among" and insert --used to screen for hybridomas producing anti-OCIF antibodies.--;

Line 15, delete "them, EIA is simple and easy to operate" and insert --EIA is a simple assay which is easy to perform--;

Line 16, delete the line in its entirety and insert --therefore generally used. The desired antibody can be--;

Line 17, delete "Thus obtained hybridoma" and insert --using EIA and purified OCIF. Hybridomas obtained thereby--; delete "the";

Line 18, delete "method" and insert --methods--;

Line 19, delete "using the" and insert --cells using--;

Line 20, delete "method" and insert --methods--; after "hybridoma" insert --cells--; delete "to" and insert --into live--;

Line 21, after "by" delete "the";

Line 22, delete "obtained";

Line 23, after "antibody" insert --obtained--; delete "for determination of" and insert --to determine--; and

Line 24, delete "for purification of OCIF." and insert --to purify OCIF protein.--.

Page 11, Line 1, delete "to" and insert --for--;

Line 2, delete "By (using)";

Line 3, delete "this assay system," and insert --This assay system is useful for determining--;

Line 4, delete the line in its entirety and insert --blood and ascites.--;

Line 5, delete the line in its entirety and insert --The present invention provides agents, containing OCIF as an--;

Line 6, delete "are provided by the present invention." and insert --ingredient, that are useful for treating bone diseases.--;

Line 7, after "of" insert --the--;

Line 8, after "weeks" insert --of--;

Line 10, after "by" insert --the--;

Line 11, before "mechanical" insert --the--;

Line 13, delete "ingredients" and insert --ingredient--; after "in" insert --bone diseases--;

Line 14, delete "bone diseases such as"; delete "osteoarthritis," and insert --osteoarthritis--;

Line 15, delete "The";

Line 16, delete "to establish" and insert --in the--; delete "the" and insert --bone--;

Line 17, delete "the"; delete "ingredients" and insert --ingredient--;

Line 19, delete "efficacious" and insert --effective--; and

Line 20, delete "human" and insert --humans--; delete "the".

Page 12, Line 1, delete "the" and insert --a--; delete "efficacious" and insert --effective--;

Line 2, before "pharmaceutically" insert --a--; delete "carriers." and insert --carrier.--;

Line 4, after "compounds" insert a comma --,--;

Line 6, delete the line in its entirety and insert --activators for injection, pH adjusters, buffers, stabilizers,--;

Line 7 - Line 23: delete the lines in their entirety.

Page 13, Delete the page in its entirety.

Page 14, Line 1 to Line 19, delete the lines in their entirety.

Line 22, delete "however," and insert --though--; delete "to the" and insert --thereto.--; and

Line 23, delete "examples.".

Page 15, Line 6, delete "under" and insert --in--;

Line 9, delete the comma ",";

Line 18, after "from" insert --a--;

Line 20, delete "D_3, and each test sample," and insert --D_3 and a test sample--; delete "to" and insert --into--;

Line 21, after "of" insert --a--;

Line 22, delete "further" and insert --maintained--; and

Line 23, delete "continued".

Page 16, Line 1, delete "starting cultivation." and insert --cultivation began.--; delete "after washing" and insert --the plates were washed--;

Line 2, delete "the plates"; delete "saline," and insert --and the--;

Line 3, delete "temperature, and then osteoclast" and insert --temperature. Osteoclast--;

Line 4, delete "for";

Line 6, delete "The decrease" and insert --A decrease in the number--;

Line 11, delete "The"; delete "filtrated with" and insert --filtered using a--;

Line 13, after "three" insert --30 liter--; delete "(30 1)";

Line 16, before "heparin" insert --the--;

Line 18, delete "as"; and

Line 22, after "overnight" delete ",".

Page 17, Line 4, delete "as";

Line 10, after "with" insert --a--;

Line 11, delete "Each" and insert --Every--; delete "number" and insert --numbers--;

Line 12, delete "was pooled" and insert --were pooled--; delete "Each"; before "of" insert --each--;

Line 13, delete "from";

Line 14, delete "The fractions from 21 to 30" and insert --Fractions 21 to 30,--;

Line 15, delete the line in its entirety and insert --activity, were pooled and designated sample 4.--;

Line 17, delete "fraction from" and insert --fractions--;

Line 18, after "to" insert --a--; and

Line 21, after "with" insert --a--.

Page 18, Line 1, delete "was" and insert --were--;

Line 2, delete "was" and insert --, were--;

Line 3, delete "was designated as" and insert --designated--;

Line 5, delete "was" and insert --were--;

Line 11, delete "The fractions number" and insert --Fractions--;

Line 12, after "NaCl" insert a comma --,--;

Line 14, delete "from 49 to" and insert --49 and--;

Line 17, delete "of" (second occurrence); after "with" insert --a--; and

Line 20, delete "peak 6 and the peak" and insert --peaks 6 and--.

Page 19, Line 11, delete "(6 and 7) with OCIF activity" and insert --with OCIF activity (peaks 6 and 7)--.

Page 20, Line 2, delete "were" and insert --are--;

Line 3, after "apparent" insert --molecular weight of--; delete "protein" and insert --sample--;

Line 7, delete "protein." and insert --sample.--; and

Line 14, delete "were" and insert --are--.

Page 21, Line 6, delete "No. 51-70 of blue-5PW fraction was" and insert --fractions 50 to 70 of the blue-5PW fractions were--;

Line 7, delete "was";

Line 8, delete "of";

Line 11, delete "peak 6 and peak" and insert --peaks 6 and--;

Line 12, delete "of" and insert --from--;

Line 14, delete "protein" and insert --proteins--; delete "N-terminal" and insert --the N-terminus--;

Line 15, delete "So, internal" and insert --Internal--;

Line 16, after "were" insert --therefore--;

Line 17, delete "of" and insert --from--; delete "peak 7" and insert --7,--; after "C4-HPLC" insert a comma --,--;

Line 20, after "each" insert --of the--; delete "mixture was" and insert --mixtures were--;

Line 21, delete "a"; after "Each" delete "the"; and

Line 22, delete "was".

Page 22, Line 3, after "vacuum" delete the comma --,--;

Line 10, after "with" insert --a--; after "gradient" insert --of--;

Line 13, delete "were" and insert --are--; delete "Sequence" and insert --SEQ. ID Nos. 1-3--;

Line 14, delete "Numbers 1-3";

Line 16, before "nucleotide" insert --the--;

Line 18, delete "by"; and

Line 19, after "using" insert --a--.

Page 23, Line 1, delete "sequence numbers" and insert --SEQ. ID Nos.--;

Line 2, after "2F" insert --(SEQ. ID No. 107)--;

Line 5, after "3R" insert --(SEQ. ID No. 108)--;

Line 10, after "2F" insert --(SEQ. ID No. 107)--;

Line 15, after "3R" insert --(SEQ. ID No. 108)--;

Line 20, after "of" insert --an--; and

Line 21, after "using" insert --a--.

Page 24, Line 1, after "7-i)" insert a comma --,--;

Line 3, delete "the";

Line 5, delete "with the conditions as follows;" and insert --using the following conditions:--;

Line 15, delete "sec annealing" and insert --sec, annealing--;

Line 16, after "amplification," insert --a--;

Line 17, delete "size of" and insert --sizes of the--; and

Line 18, delete "About" and insert --An approximately--.

Page 25, Line 2, delete "in the plasmid," and insert --into the plasmid--; after "using" insert --a--;

Line 3, delete "by" and insert --of--;

Line 4, before "DH5" insert --strain--; after "with" insert --the--;

Line 6, delete "the"; delete "method." and insert --methods.--;

Line 7, before "OCIF" insert --the--; after "using" insert --a--;

Line 11, delete "sequence number" and insert --SEQ. ID Nos.--;

Line 12, delete "N- or C- terminal side in the" and insert --the amino or carboxyl terminus of the 132--;

Line 13, delete "of the 132 amino acid polypeptide";

Line 14, delete "sequence number" and insert --SEQ. ID No.--;

Line 15, delete "the polypeptide." and insert --OCIF.--;

Line 22, after "using" insert --a--; and

Line 23, after "using" insert --a--.

Page 26, Line 5, after "using" insert --a--;

Line 7, after "7-i)" insert a comma --,--; before "EcoRI" insert --An--;

Line 8, after "from" delete "the"; after "adaptor" insert --DNA--;

Line 11, delete "with the adaptor was inserted in" and insert --comprising the adaptor was legated into a--;

Line 12, after "at" insert --the--;

Line 13, after "using" insert --a--;

Line 14, delete "and" and insert --, yielding a--; delete "was prepared";

Line 17, delete "infected to E. Coli," and insert --used to infect E. coli strain--;

Line 19, delete "on the" and insert --onto--;

Line 21, after "(Amersham)" insert --membranes--; after "of" insert --the--; and

Line 22, delete "the".

Page 27, Line 1, delete "the standard protocol" and insert --standard methods--; delete "on" and insert --onto--;

Line 2, after "in" delete "the";

Line 5, before "denatured" insert --of--;

Line 8, delete "about 1.6 kb" and insert --a--;

Line 9, after "insert" insert --of about 1.6kb--;

Line 10, delete "and the infected into E. Coli" and insert --was used to infect E. coli strain--;

Line 11, delete "a" and insert --the--; delete "of" and insert --in the--;

Line 13, delete "1OCIF" and insert --λOCIF--;

Line 20, delete "picking up" and insert --lifting--;

Line 21, delete "to" and insert --in the--; and

Line 24, delete "transfered" and insert --transferred--.

Page 28, Line 2, delete "the standard protocol" and insert --standard methods--;

Line 7, after "using" insert --a--;

Line 8, after "T7" delete "primers";

Line 10, delete "sequence numbers" and insert --SEQ. ID Nos.--;

Line 11, delete "sequence number" and insert --SEQ. ID No.--;

Line 12, delete "sequence number" and insert --SEQ. ID No.--;

Line 16, after "pBKOCIF" insert a comma --,--; after "cDNA" insert a comma --,--;

Line 17, delete the commas (both occurrences) ",";

Line 18, after "electrophoresis" delete ",";

Line 19, after "using" insert --a--;

Line 20, delete the line in its entirety and insert --insert was ligated into the--;

Line 21, after "(Invitrogen)" insert --using DNA ligation kit ver. 2 (Takara Shuzo), and--; after "enzymes" delete ","; and

Line 22, delete "E. coli." and insert --E. coli strain--.

Page 29, Line 2, after "using" insert --a--;

Line 3, delete ",";

Line 4, delete "was used in the expreriments" and insert --for use in the experiments--;

Line 5, delete "the" and insert --OCIF--;

Line 6, delete the comma ",";

Line 7, before "prepared" insert an open paren --(--;

Line 8, delete "in" and insert --into--; delete "the" and insert --a--;

Line 11, delete the comma ",";

Line 12, delete " and were" and insert --,--;

Line 17, delete "the transfected cells were incubated" and insert --incubation--;

Line 20, delete "mice, 17 days-old," and insert --17 day old mice--;

Line 22, delete "D_3, and each" and insert --D_3 and a--; and delete "inoculatd" and insert --inoculated--.

Page 30, Line 5, delete "then";

Line 7, delete "The decrease of" and insert --A decrease in--; and

Line 8, delete "As result, the" and insert --The--.

Page 31, Line 4, delete "of";

Line 5, delete "with" and insert --using a--;

Line 6, delete "50 ml of a" and insert --a 50 ml--;

Line 9, after "with" insert --a--;

Line 10, after "and" insert --8 ml--; delete "(8 ml)";

Line 12, delete "OCIF active fraction (112 ml)" and insert --An OCIF active 112 ml fraction,--; after "NaCl" insert a comma --,--;

Line 18, after "with" insert --a--;

Line 19, delete a comma ","; after "and" insert --0.5 ml--; delete (0.5 ml);

Line 22, delete "On SDS-PAGE under reducing conditions, a" and insert --A--; and

Line 23, delete ", under" and insert --by SDS-PAGE under reducing conditions.--.

Page 32, Line 1, delete "non-reducing conditions, bands" and insert --Bands--; delete "an apparent" and insert --apparent molecular weights of--;

Line 2, after "32" insert --under non-reducing conditions--;

Line 3, delete "fraction from" and insert --from fractions--;

Line 5, after "Lowry" insert a comma --,--;

Line 10, after "enzymes" delete the comma ",";

Line 11, delete "an"; delete the comma ",";

Line 12, after "using" insert --a--;

Line 14, delete the comma ",";

Line 16, delete the comma ","; after "using" insert --a--;

Line 18, after "using" insert --a--;

Line 19, after "using" insert --a--;

Line 20, delete "coli." insert --coli strain--; and

Line 21, delete "The" and insert --A--.

Page 33, Line 1, after "of" insert --the--;

Line 3, delete "prepared in the" and insert --prepared in--;

Line 4, delete "the";

Line 5, delete "method." and insert --methods.--;

Line 6, delete "chrolide" and insert --chloride--;

Line 7, after "to" insert --the--;

Line 15, delete "to" and insert --into--;

Line 22, after "using" insert --a--; and delete "condition" and insert --the conditions--.

Page 34, Line 3, delete "Then the" and insert --The--; after "were" insert --then--;

Line 4, delete "in" and insert --into--;

Line 14, delete "the" and insert --a--; delete "amount" and insert --amounts--;

Line 15, after "OCIF," insert --named--;

Line 18, delete "the clone (5561)" and insert --clone 5561--; and

Line 20, delete "to".

Page 35, Line 2, delete "cells-conditioned" and insert --cell-conditioned--;

Line 3, delete "CHOcells-conditioned" and insert --CHO cell-conditioned--; delete "EXAMPL" and insert --EXAMPLE--;

Line 4, delete "of"; before "0.22" insert --a--;

Line 5, delete "Milipore" and insert --Millipore--;

Line 8, after "with" insert --a--;

Line 9, after "and" insert --8 ml--; delete "(8";

Line 10, delete "ml)";

Line 11, delete "Active" and insert --An active--;

Line 13, delete "of";

Line 14, delete "a" and insert --an--;

Line 17, after "with" insert --a--;

Line 18, delete the comma ",";

Line 19, delete "was" and insert --were--;

Line 20, delete "On SDS-PAGE";

Line 21, delete "a" and insert --A--; after "with" insert --an--; after "apparent" insert --molecular weight of--;

Line 22, delete ", under non-reducing conditions, bands" and insert --using SDS-PAGE under reducing conditions. Bands--;

Line 23, after "apparent" insert --molecular weights of--; and before "were" insert --using SDS-PAGE under non-reducing conditions--.

Page 36, Line 1, after "fraction," insert --from fractions--;

Line 3, delete "obtained when" and insert --obtained, as--.

Page 37, Line 8, delete "sequence No." and insert --SEQ. ID No.--;

Line 9, delete "the 22th amino" and insert --glutamine, located at position 22--;

Line 10, delete the line in its entirety and insert --from the translation start Met, as shown in SEQ. ID No.--;

Line 11, delete "number";

Line 13, delete "was undetectable." and insert -- could not be determined.--;

Line 14, delete "converting from" and insert --the conversion of--;

Line 15, delete the line in its entirety and insert --cell culture or purification steps.--;

Line 18, delete "from" and insert --in--;

Line 20, delete "sample was" and insert --samples were--; and

Line 23, delete "in" and insert --of a--.

Page 38, Line 1, delete "mice, 17 days-old," and insert --17 day old mice--;

Line 2, delete "to" and insert --into--; delete "in" and insert --of a--;

Line 4, delete "a" and insert --an--; delete "mesuring" and insert --measuring--;

Line 5, delete "The" and insert --A--;

Line 6, delete "of" and insert --in--; after "as" insert --an indication of--; delete "The" and insert --A--;

Line 7, delete "of" and insert --in--;

Line 8, delete "In detail," and insert --Briefly,--;

Line 11, after "590" insert a comma --,--;

Line 12, after "using" insert --a--;

Line 14, delete "was" and insert --were--;

Line 15, delete "The decrease of" and insert --A decrease in--;

Line 16, delete "of the" and insert --(the--;

Line 17, delete "which were"; and delete "OCIF" and insert --OCIF)--.

Page 39, Line 3, delete "in the concentration" and insert --at concentrations--; delete "higher" and insert --greater.--;

Line 6, delete "Effect" and insert --The effect--;

Line 9, delete "In detail," and insert --Briefly, samples of--; delete "sample was" and insert --were--;

Line 10, delete "of";

Line 11, delete the comma ","; after "each" insert --of--;

Line 12, delete "in" and insert --of--;

Line 13, delete ";" and insert --at--;

Line 14, delete "FBS," and insert --FBS--; delete "ddy mice, 8 weeks-old, ;" and insert --8 week old ddy mice at--;

Line 15, delete "to" and insert --into--; delete "in 96-well plates" and insert --of a 96-well plate--;

Line 17, delete "with a kit for" and insert --using an--; after "phosphatase" insert --kit--;

Line 18, delete "The decrease of" and insert --A decrease in--;

Line 19, after "taken" insert --as an indication--; delete "of" and insert --in--;

Line 21, delete the line in its entirety and insert --are shown in Table 6 (rOCIF(E) and rOCIF (C)) and Table 7 (rOCIF(E) and--; and

Line 22, delete "nOCIF" and insert --nOCIF)--.

Page 40, Line 14, delete "in the concentration" and insert --at concentrations--; delete "higher" and insert --greater--;

Line 15, delete "from" and insert --in--; and

Line 17, delete "Effect" and insert --The effect--.

Page 41, Line 1, delete "In detail, each the" and insert --Briefly, samples of each of--; delete "sample";

Line 2, delete "was" and insert --were--;

Line 3, after "each" insert --of--; after "to" insert --the wells of--;

Line 4, delete "ddy mice, 17 days-old," and insert --17 day old ddy mice--;

Line 6, delete "to" and insert --into--; delete "in" and insert --of a--; delete "plates" and insert --plate--;

Line 7, delete "aceton" and insert --acetone--;

Line 8, delete "a kit for" and insert --an--; after "phosphatase" insert --kit--;

Line 10, delete "The" and insert --A--; delete "of" and insert --in--; after "as" insert --an indication of--;

Line 11, delete "of" and insert --in--;

Line 20; please delete "in the concentration" and insert --at concentrations--; and delete "higher" and insert --greater--.

Page 42, Line 1, delete "Effect" and insert --The effect--;

Line 3, delete "In detail, each" and insert --Briefly, a sample of each of--; delete "sample was" and insert --were--;

Line 5, delete "the"; after "in" insert --a--;

Line 6, delete "plates." insert --plate.--;

Line 7, delete ";" and insert --at--;

Line 8, delete "ddy mouse, 8 weeks-old, ;" and insert -- 8 week old ddy mouse, at--;

Line 9, delete "to" and insert --into--; delete "in" and insert --of a--; delete "plates" and insert --plate--;

Line 12, after "under" insert --a--;

Line 13, after "as" insert --an indication of--;

Line 20, delete "in the concentration" and insert --at concentrations--; and delete "higher" and insert --greater.--.

Page 43, Line 2, delete "would be able to" and insert --could--; delete "treatment of the" and insert --treating--;

Line 3, delete "with" insert --due to--; delete "which" and insert --that--;

Line 4, delete "which" and insert --that--;

Line 11, after "with" insert --a--;

Line 12, delete "Each the" and insert --The--;

Line 13, delete "was" and insert --were--;

Line 14, delete line in its entirety and insert --each lyophilized.--;

Line 16, before "molecular" insert --the--;

Line 18, after "using" insert --a--; and

Line 20, delete "vaccum, respectively." and insert --vacuum.--.

Page 44, Line 2, delete "Figure 6 and Figure 7." and insert --Figures 6 and 7, respectively.--;

Line 5, delete "in" (second occurrence) and insert --under--;

Line 8, before "molecular" insert --the--;

Line 9, after "same" insert -- (60KD)--;

Line 11, after "same" insert -- (120KD)--;

Line 13, delete "Remove" and insert --Removal of the--; delete "Mesuring" and insert --measuring the--; and

Line 16, after "using" insert --a--.

Page 45, Line 1, delete the comma ",";

Line 4, after "each" insert --of--; and

Line 6, after "each" insert --of the--.

Page 46, Line 2, delete "squences" and insert --sequences--;

Line 3, delete "which is inserted" and insert --comprising--;

Line 3, delete "to" and insert --into plasmid--;

Line 4, delete "from one of some purified positive phage";

Line 5, delete "And more" and insert --Further--;

Line 8, delete "the";

Line 9, after "using" insert --a--;

Line 10, delete "used primers" and insert --primers used--;

Line 11, delete "primers" (first occurrence) and insert a comma --,--;

Line 14, delete "sequence number" and insert --SEQ. ID No.--;

Line 15, delete "the sequence number" and insert --SEQ. ID No.--;

Line 16, delete "the sequence number" and insert --SEQ. ID No.--;

Line 17, delete "the sequence number" and insert --SEQ. ID No.--;

Line 18, delete "the sequence number" and insert --SEQ. ID No.--;

Line 20, delete "the sequence number" and insert --SEQ. ID No.--; after "shown in" delete "the";

Line 21, delete "sequence number" and insert --SEQ. ID No.--;

Line 22, delete "the sequence number" and insert --SEQ. ID No.--; and

Line 23, after "and are" insert --briefly--; and delete "in brief".

Page 47, Line 1, before "OCIF2" insert --The--;

Line 2, after "in" insert --the--;

Line 2, delete "sequence number" and insert --SEQ. ID No.--;

Line 3, after "Accordingly" insert a comma --,--;

Line 5, delete "sequence number" and insert --SEQ. ID No.--;

Line 7, before "OCIF3" insert --The--;

Line 7, after "in" insert --the--;

Line 8, delete "sequence number" and insert --SEQ. ID No.--;

Line 9, after "Accordingly" insert a comma --,--; after "and" insert --an--;

Line 10, delete "sequence number" and insert --SEQ. ID No.--;

Line 11, delete "have" and insert --has--;

Line 12, delete "secreted" and insert --secretion of--;

Line 13, after "in" insert --the--;

Line 13, delete "sequence number" and insert --SEQ. ID No.--;

Line 15, after "Accordingly" insert a comma --,--;

Line 17, delete "sequence number" and insert --SEQ. ID No.--;

Line 19, after "in" insert --the--;

Line 19, delete "sequence number" and insert --SEQ. ID No.--;

Line 21, after "in" insert --the--;

Line 21, delete "sequence number" and insert --SEQ. ID No.--;

Line 23, after "Accordingly" insert a comma --,--; and

Line 24, after "sequence number" insert --SEQ. ID No.--.

Page 48, Line 4, delete "which is the" and insert --comprising--; after "of" insert --the--;

Line 5, after "in" insert --the--; delete "sequence" and insert --SEQ. ID No.--;

Line 6, delete "number";

Line 7, after "Accordingly" insert a comma --,--;

Line 8, delete "sequence" and insert --SEQ ID No. 5).--;

Line 9, delete the line in its entirety.

Line 11, before "OCIF5" (first occurrence) insert --The--; before "OCIF" (second occurrence) insert --the--;

Line 12, delete "sequence number" and insert --SEQ. ID No.--;

Line 13, after "Accordingly" insert a comma --,--; after "and" insert --an--;

Line 14, delete "sequence number" insert --SEQ. ID No.--;

Line 15, delete "have" and insert --has--;

Line 16, delete "secreted" and insert --secretion of--;

Line 17, before "OCIF5" insert --The--;

Line 18, delete "sequence number" insert --SEQ. ID No.--;

Line 20, after "Accordingly" insert a comma --,--;

Line 21, delete "sequence" and insert --SEQ. ID No.--; and

Line 22, delete "number 5).".

Page 49, Line 3, delete "The Plasmid" and insert --Plasmids--; delete "was" and insert --were--;

Line 5, delete the comma ",";

Line 6, delete the comma ",";

Line 7, after "using" insert --a--;

Line 8, after "using" insert --a--;

Line 10, delete the comma ","; delete "coli." and insert --coli strain--;

Line 13, delete the comma ",";

Line 14, delete "an";

Line 15, after "using" insert --a--;

Line 16, after "using" insert --a--;

Line 17, delete "the" and insert --an--;

Line 18, delete the comma ","; after "E. coli" insert --strain--;

Line 21, delete "was"; after "with" insert --the--; delete the comma ","; and

Line 23, delete the comma ","; and after "using" insert --a--.

Page 50, Line 1, after "with" insert --the--; delete the comma ",";

Line 5, delete "an"; delete the comma ","; after "using" insert --a--;

Line 7, after "using" insert --a--; delete "E. coli." and insert --E. coli strain--;

Line 9, delete "obtained transformants" and insert --transformants obtained--; delete "variants" and insert --variant--;

Line 11, delete "column" and insert --columns--;

Line 11, delete “variants” and insert --variant--;

Line 13, delete “expreriments” and insert --experiments--;

Line 16, delete “plasmid,” and insert --plasmids--;

Line 17, delete “prepared”; and

Line 20, delete “a”.

Page 51, Line 5, delete “a”;

Line 5, before “DNA” insert --A--;

Line 7, after “using” insert --a--;

Line 12, before “DNA” insert --A--;

Line 13, after “using” insert --a--;

Line 14, delete “The” and insert --This--;

Line 16, delete “of” (second occurrence) and insert --from a--;

Line 18, delete “for” and insert --in--;

Line 20, after “E. coli” insert --strain--;

Line 21, delete “was” and insert --were--;

Line 22, delete “to the cells”;

Line 23, delete “was added”; and after “NaCl)” insert --was added to the cells--;

Page 52, Line 3, delete “individually” and insert --each--;

Line 4, delete “each”;

Line 4, delete “of” (second occurrence);

Line 10, after “with” insert --a--; and

Line 14, after “with” insert --a--.

Page 53, Line 13, delete “SEQUENCE NO:” and insert --SEQ. ID Nos.--;

Line 14, delete "as follows";

Line 16, after "min" (first occurrence) insert a comma --,--;

Line 18, delete "size" and insert --sizes--;

Line 18, delete "prodcts was" and insert --products were--;

Line 19, delete "using" and insert --of the--; delete "solution" and insert --solutions--; and

Line 20, after "using" insert --an--.

Page 54, Line 16, delete "size" and insert --sizes--; delete "prodcts was" and insert --products were--; and

Line 19, delete "mutation" and insert --mutations--.

Page 55, Line 7, delete "was" (second occurrence) and insert --were--;

Line 9, delete "with" and insert --using a--;

Line 11, delete "as";

Line 12, delete "of" (fourth occurrence) and insert --from a--;

Line 13, after "and" insert --the--;

Line 14, delete "E. coli DH5 α" and insert --E. coli strain DH5α--;

Line 16, delete "a";

Line 19, delete "which is";

Line 21, delete "with" and insert --using a--; and

Line 24, delete "of" and insert --from a--.

Page 56, Line 1, after "and" insert --the--;

Line 1, after "E. coli" insert --strain--;

Line 3, delete "a" (second occurrence);

Line 8, delete "with" and insert --using a--;

Line 10, delete "as";

Line 11, delete "of" and insert --from a--;

Line 12, after "and" insert --the--;

Line 12, after "E. coli" insert --strain--;

Line 14, delete "a" (second occurrence);

Line 19, delete "with" and insert --using a--;

Line 21, delete "was" (second occurrence) and insert --were--; and

Line 23, delete "with" and insert --using a--.

Page 57, Line 2, delete "of" (fourth occurrence) and insert --from a--;

Line 3, after "and" insert --the--;

Line 4, after "E. coli" insert --strain--;

Line 6, delete "a";

Line 13, delete "with" and insert --using a--;

Line 15, delete "was" (second occurrence) and insert --were--;

Line 17, delete "with" and insert --using a--;

Line 20, delete "of" (fourth occurrence) and insert --from a--;

Line 21, after "and" insert --the--;

Line 22, after "E. coli" insert --strain--; and

Line 23, delete "a" (second occurrence).

Page 58, Line 10, delete "a";

Line 10, delete "was" and insert --were--;

Line 16, delete "of" (second occurrence) and insert --from a--;

Line 17, after "and" insert --the--;

Line 18, after "coli" insert --strain--; and

Line 22, delete "plasmide" and insert --plasmids--.

Page 59, Line 4, delete "of" (second occurrence);

Line 6, delete "and" and insert --or--;

Line 7, delete "SEQUENCE NO:" and insert --SEQ. ID No.--;

Line 12, delete "SEQUENCE NO:" and insert --SEQ. ID Nos.--; and

Line 12, after "40-53" delete the comma --,--.

Page 60, Line 2, delete "fragment" and insert --fragments--;

Line 6, delete "which is";

Line 8, delete "with" and insert --using a--;

Line 10, delete "was" (second occurrence) and insert --were--;

Line 12, delete "with" and insert --using a--;

Line 15, delete "of" (third occurrence) and insert --from a--;

Line 16, after "and" insert --the--;

Line 17, after "E. coli" insert --strain--;

Line 18, delete "a" (second occurrence);

Line 23, delete "with" and insert --using a--;

Page 61, Line 1, delete "as" (first occurrence);

Line 3, after "and" insert --the--; after "E. coli" insert --strain--;

Line 6, delete "DNA ." and insert --DNA.--;

Line 10, delete "with" and insert --using a--;

Line 12, delete "as";

Line 13, delete "of" and insert --from a--;

Line 14, after "and" insert --the--; after "E. coli" insert --strain--; and

Line 21, delete "with" and insert --using a--.

Page 62, Line 2, delete "as"; delete "was" (second occurrence) and insert --were--;

Line 4, delete "with" and insert --using a--;

Line 6, delete "as";

Line 8, delete "of" and insert --from a--;

Line 8, after "and" insert --the--;

Line 9, after "E. coli" insert --strain--; and

Line 11, delete "a";

Line 16, delete "with" and insert --using a--;

Line 19, delete "of" and insert --from a--;

Line 20, after "and" insert --the--;

Line 20, after "E. coli" insert --strain--; and

Line 22, delete "a" (second occurrence).

Page 63, Line 3, delete "with" and insert --using a--;

Line 6, delete "of" and insert --from a--;

Line 7, after "and" insert --the--;

Line 7, after "E. coli" insert --strain--;

Line 9, delete "a" (second occurrence); and

Line 15, after "containing" insert --the--.

Page 64, Line 1, delete "of" and insert --from a--;

Line 1, after "and" insert --the--;

Line 2, after "E. coli" insert --strain--;

Line 4, delete "a" (second occurrence);

Line 12, delete "of";

Line 15, delete "SEQUENCE NO:" and insert --SEQ. ID No.--; and

Line 20, delete "SEQUENCE NO:" and insert --SEQ. ID Nos.--.

Page 65, Line 3, delete "with" and insert --using a--;

Line 5, delete "as";

Line 7, delete "of" and insert --from a--; after "and" insert --the--;

Line 8, after "E. coli" insert --strain--;

Line 10, delete "a";

Line 12, after "pSK-OCIF-CL" insert a period --.--;

Line 13, after "PCR" insert --reaction--; and

Line 15, after "OCIF-CCR3" insert --were as follows:--.

Page 66, Line 3, delete "with" and insert --using a--;

Line 6, delete "SEQUENCE NO:" and insert --SEQ. ID Nos.--;

Line 12, delete "an";

Line 14, delete "The size of the PCR products was confirmed on an agarose gel.";

Line 15, after "using" insert --an--; and

Line 21, after "containing" insert --the--.

Page 67, Line 3, delete "CC R3" and insert --CCR3--;

Line 14, delete "isolatedand" and insert --isolated and --;

Line 16, delete "of" (second occurrence);

Line 18, delete "of" (second occurrence) and insert --from a--;

Line 19, after "and" insert --the--; and

Line 19, after "E. coli" insert --strain--.

Page 68, Line 1, after "in" (first occurrence) insert --the--;

Line 2, after "plasmid," insert --the--; delete "were" and insert --was--;

Line 7, delete "truncation" and insert --truncations--;

Line 8, delete "truncation" and insert --truncations--;

Line 9, delete "truncation" and insert --truncations--; before "OCIF" insert --An--;

Line 10, delete "of"; delete "are" and insert --were--;

Line 11, delete "of Leu-Val" and insert --(Leu-Val)--; before "OCIF" insert --An--;

Line 12, delete "of" (first occurrence); delete "are" and insert --were--; delete "of Ser-Leu-Asp" and insert --(Ser-Leu-Asp)--;

Line 13, before "OCIF" insert --An--; delete "of";

Line 14, delete "are" and insert --were--; delete "OCIF muatant" and insert --An OCIF mutant--;

Line 15, delete "of" (first occurrence); delete "are" and insert --were--; delete "of Leu-Val" and insert --(Leu-Val)--;

Line 17, delete "SEQUENCE NO:" and insert --SEQ. ID No.--;

Line 18, delete "was" and insert --were--; delete "one of the";

Line 19, delete "restriction enzymes,"; delete ", and" and insert --or--;

Line 20, delete ", and";

Line 21, delete "Ends" and insert --The ends--;

Line 22, after "in" (second occurrence) insert --a--; and

Line 23, delete "volumes" and insert --volume--.

Page 69, Line 2, delete "of" and insert --from a--;

Line 4, after "E. coli" insert --strain--;

Line 8, delete "for";

Line 9, delete "pSK-OCIF- CSph" and insert -- pSK-OCIF-CSph--;

Line 10, delete "of";

Line 11, after "containing" insert --the--;

Line 13, delete "contain" and insert -- contained--; delete "pSK-OCIF- CSph" and insert --pSK-OCIF-CSph--;

Line 14, delete "and" and insert --or--; delete "as";

Line 18, delete "of" (second occurrence) and insert --from a--;

Line 19, after "and" insert --the--;

Line 20, after "coli" insert --strain--;

Line 22, after "which " insert --the--;

Line 23, please delete "is" and insert --was--; and

Line 25, delete "and" and insert --or--.

Page 70, Line 3, delete "Preparetion" and insert --Preparation--; after "(" insert --a--;

Line 5, after "by" insert --using--; delete "column" and insert --columns--;

Line 13, delete "A 24-well plate was used for the DNA";

Line 14, delete "transfection.";

Line 15, delete "the" and insert --a 24 well--;

Line 17, delete "Mixture of an" and insert --A mixture of the--;

Line 19, delete "a CO_2 incubator" and insert --5% CO_2--;

Line 21, delete "48 more" and insert --a further 48--; delete "the CO_2 incubator" and insert --5% CO_2--;

Line 22, delete "for assay" and insert --in assays--;

Line 23, delete "SEQUENCE NO:" and insert --SEQ. ID Nos.--; and

Line 24, delete "SEQUENCE NO:" and insert --SEQ. ID No.--.

Page 71, Line 2, delete "Antigen" and insert --The Antigen--;

Line 3, delete "specific" and insert --the--; and

Line 4, delete "the" and insert --each--; delete "the".

Page 72, Line 4, after "OCIF" insert a semicolon -;--;

Line 5, after "50%" please insert a semicolon --;--;

Line 7, after "activity" insert a period --.--;

Line 8, delete "western" and insert --Western--;

Line 10, delete "the" and insert --each--;

Line 11, delete "bromo phenol" and insert -- bromophenol --;

Line 12, after ")" insert a comma --,--; delete "a"; delete "polyacryl amide" and insert --polyacrylamide--;

Line 16, delete "peroxidase labeled" and insert -- peroxidase-labeled --;

Line 18, after "using" insert --an--;

Line 20, after "exclusively" insert --a--; after "for" insert --the--; and

Line 21, after "CC" insert --mutants--; delete "an".

Page 73, Line 3, delete "resare" and replace with "residues are";

Line 4, delete "SEQUENCE NO:" and insert --SEQ. ID No.--.

Page 74, Line 5, delete "purchased from STRATAGENE" and insert --(Stratagene)--;

Line 8, delete "also were" and insert --were also--;

Line 11, delete "on" and insert --onto--;

Line 16, delete "successively for one minute each" and insert --each one--;

Line 17, after "7.5)" insert --, successively for one minute--; delete "wet" and insert --wetted--; and

Line 19, delete "on" and insert --onto--; delete "in" and insert --using a--.

Page 75, Line 7, delete "PFOTO" and insert --pFOTO--; and

Line 13, delete "on" and insert --onto--.

Page 76, Line 8, delete "the";

Line 10, delete "the";

Line 13, delete "determination of the" and insert --determining their--;

Line 14, delete the comma ",";

Line 15, delete "these from" and insert --therefrom--;

Line 16, delete "pairs" and insert --pair--; after "using" insert --a--; and

Line 20, after "(STRATEGENE)" insert a comma --,--.

Page 77, Line 3, after "and" insert --a--; delete "of";

Line 5, delete "in" and insert --into--;

Line 8, delete "in" (second occurrence) and insert --into a--;

Line 11, delete "applied" and insert --separated--;

Line 11, delete "in" and insert --into--;

Line 15, delete "pBS6 H1.1" and insert -- pBS6H1.1--;

Line 17, after "using" insert --a--;

Line 18, after "and" insert --a--;

Line 22, delete "the";

Line 23, after "Nucleotide" insert --The nucleotide--; delete "was" and insert --is--; and

Line 24, delete "Sequence No" (first occurrence) and insert --SEQ. ID No.-- delete "Sequence No" (second occurrence) and insert --SEQ. ID No.--.

Page 78, Line 2, delete "of nucleotides"; delete "sequence" and insert --SEQ. ID--;

Line 3, delete "sequence" and insert --SEQ. ID No.--;

Line 8, delete "for" and insert --in--; delete "Three male JW rabbits (Kitayama";

Line 9, delete "the line in its entirety and insert --For--;

Line 10, after "immunization," insert --an--;

Line 11, delete "The" and insert --Three--;

Line 12, delete "the interval of"; after "week" insert --intervals--;

Line 13, delete "The rabbits were injected six times at the interval";

Line 14, delete "of seven days subcutaneously";

Line 15, delete "separated" and insert --isolated--;

Line 17, delete "40 w/v %," and insert --40% w/v, the--;

Line 18, delete ". Precipitate" and insert --The precipitate--;

Line 20, delete "resulting" and insert --resultant--;

Line 22, delete "Elutes were" and insert --The eluate was immediately--; and

Line 23, delete "immediately and were" and insert --and--.

Page 79, Line 2, delete "peroxidase labeled" and insert --peroxidase-labeled--; after "using" insert --an--;

Line 6, delete "separeted by" and insert --separated using a--;

Line 6, delete "Protein pool" and insert --The protein pool was--;

Line 7, delete "maleimide activated" and insert --maleimide-activated--; delete "was" and insert --and--;

Line 12, delete "4C" and insert --4°C--;

Line 14, delete "of";

Line 16, delete "peroxidase labeled" and insert -- peroxidase-labeled --;

Line 17, delete "temperture" and insert --temperature--; and

Line 21, delete "standared" and insert --standard--; delete "was" and insert --is--.

Page 80, Line 2, after "of" insert --a--;

Line 3, after "from" insert --the--; delete "fibroblasts" and insert --fibroblast--;

Line 4, after "IMR-90" insert --cells--;

Line 4, delete "Eample" and insert --Example--;

Line 6, delete "administrating" and insert --administering--;

Line 7, after "emulsion" insert --was--;

Line 8, delete "was administered"; delete "administration" and insert --immunization--;

Line 9, delete "taken out," and insert --removed and--;

Line 10, delete "were";

Line 11, delete "the conventinal method" and insert --conventional methods--;

Line 12, delete "hybridoma" and insert -- hybridomas--; delete "Subsequently, to check";

Line 13, delete "whether the selected hybridomas produce anti-OCIF antibody," and insert --The presence of--;

Line 14, delete "each" and insert --the--; delete "hybridomas" and insert --each hybridoma--; delete "which" and insert --. Briefly,--;

Line 15, delete "was prepared by coating"; delete "in" and insert --of a--; delete "immunoplates" and insert -- immunoplate--; after "(Nunc)" insert --was coated--;

Line 16, delete "by blocking each well" and insert --blocked--;

Line 18, after "by" insert --by limit dilution--; delete "by limit dilution";

Line 19, delete "screening using the above"; delete ". Among thus obtained" and insert --screening--;

Line 20, delete the line in its entirety and insert --Several hybridoma clones producing high levels of anti-OCIF--; and

Line 23, delete ", which was".

Page 81, Line 1, delete the comma ","; delete "to" and insert --into--;

Line 2, after "(Aldrich)" insert a comma --,--;

Line 3, delete "the transplantation and the ascites containing" and insert --transplantation, thereby obtaining--;

Line 4, delete "was obtained" and insert a period --.--;

Line 6, delete "maufacturer's" and insert --manufacturer's--; delete "That is" and insert --Briefly--;

Line 7, after "ascites" insert --fluid--; after "with" insert --an--;

Line 8, after "to" insert --a--; delete "the" (second occurrence);

Line 10, delete "obtained eluate" and insert --eluate obtained--;

Line 11, delete "obtained antibody " and insert --antibody thereby obtained--;

Line 13, after "of" insert --a--; delete "to" and insert --for--;

Line 15, delete "concentration of protein in the solution" and insert --protein concentration--;

Line 16, delete "with" and insert --was diluted to--; delete "was prepared";

Line 18, delete "diluted solution" and insert --dilute concentrations--;

Line 19, after "Thus" please insert a comma --,--;

Line 20, delete "can be" and insert --were--;

Page 82, Line 4, delete "protocol disclosed in the" and insert --kit--; delete "were" and insert --are--;

Line 5, after "to" insert --the--;

Line 6, after "IgG_{2b}," insert --subclasses--;

Line 8, delete "in" and insert --of--;

Line 13, delete "Determination" and insert --Quantitation--;

Line 14, delete ", which were";

Line 15, delete "25-iv)," and insert --25-iv--;

Line 17, delete "each combination" and insert --different combinations--;

Line 18, after "using" insert --an--; and delete "Maleimide Activiated" and insert --Maleimide-Activiated --.

Page 83, Line 2, delete "in" and insert --of a--;

Line 3, after "allowing" insert --them--;

Line 4, delete "in" and insert --of--;

Line 5, delete "then";

Line 6, delete "was";

Line 8, delete "bufer" and insert --buffer--;

Line 9, delete "in" and insert --of a--; delete "immunoplates" and insert --immunoplate--;

Line 11, delete "the"; delete "For";

Line 12, delete the line in its entirety;

Line 13, delete the line in its entirety and insert --the POD-labeled--;

Line 14, after "buffer" insert --(0.1 M Tris-HCl buffer, pH 7.4, containing 25% Blockace and 0. 1% Tween 20)--;

Line 15, delete "in" and insert --of--; delete "imunoplate" and insert --immunoplate--;

Line 16, delete "C" (second occurrence);

Line 17, delete "the";

Line 19, delete "in" and insert --of--;

Line 20, delete "were";

Line 24, delete "kinds of" and insert --different--; delete "antibody in" and insert --antibodies of--;

Page 84, Line 1, delete "a" and insert --an--;

Line 2, after "OCIF" insert --concentration--; delete "in" and insert --of--;

Line 4, after "A1G5" insert a comma --,--;

Line 5, delete "was" and insert --, is--;

Line 7, delete "Concentration" and insert --The concentration--;

Line 9, after "of" insert --the--;

Line 10, delete "in" and insert --of--;

Line 11, delete "in" and insert --of--; delete "immnuoplates" and insert --immunoplates--;

Line 12, delete "then"; delete "the";

Line 13, delete "in" and insert --of--;

Line 14, after "with" insert --the--;

Line 15, delete "the" (second occurrence);

Line 18, delete "in" and insert --of--; and

Line 23, delete "sample."

Page 85, Line 13, delete "Male" and insert --Six week old male--; delete ", 6 weeks old,"; after "of" insert --the--;

Line 16, delete "intravenous administration of vehicle" and insert --the vehicle administered intravenously--;

Line 17, delete "administered OCIF" and insert --with OCIF administered--; and

Line 18, delete "administered OCIF" and insert --with OCIF administered--.

Page 86, Line 3, delete "Decrease of" and insert --A decrease is--; delete "the animals of control groups" and insert --control animals--;

Line 5, delete "groups" and insert --group--; delete "animal" and insert --animals that--;

Line 7, after "inhibits" insert --the--;

Line 8, delete "a" and insert --an--; delete "to produce" and insert --for producing--;

Line 9, delete "has an activity to inhibit" and insert --inhibits the--;

Line 11, delete "accompanying" and insert --accompanied by--; delete "to be used"; and

Line 13, delete "microorgainsm" and insert --microorganism--.

IN THE CLAIMS:

Please cancel claims 1-31. Please add new claims 32-36 as follows:

32. An antibody having specific affinity to an osteoclastogenesis inhibitory factor protein comprising the following properties:

(a) molecular weights as determined by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) of approximately 60 kD under reducing conditions, and
approximately 60 kD (a monomer) and 120 kD (a homodimer) under non-reducing conditions;

(b) high affinity to cation-exchange resins and heparin derivatives;

(c) inhibitory activity for osteoclast differentiation and/or maturation, wherein said activity is decreased by heating said protein at about 70°C for about 10 min. or at about 56°C for about 30 min., and wherein said activity is lost by heating at about 90°C for about 10 min.; and

(d) an internal amino acid sequence as provided in SEQ. ID NOS. 1, 2 or 3.

33. The antibody of claim 32 that is polyclonal.

34. The antibody of claim 32 that is monoclonal.

35. The monoclonal antibody of claim 34 being characterized by the following properties:

a molecular weight of about 150,000, and of subclass IgG_1, IgG_{2a}, or IgG_{2b}.

36. A method of determining the concentration of an osteoclastogenesis inhibitory factor protein comprising contacting a sample suspected of containing said protein with an antibody of claims 32, 33, 34, or 35 under conditions sufficient to induce formation of protein-antibody conjugates, and detecting the amount of protein-antibody conjugates formed.

REMARKS

The Examiner required restriction of the claims in the patent application, U.S.S.N. 08/915, 004. This is a divisional application of U.S.S.N. 08/915,004, filed to pursue and elect the claims of Group III, claims 27-31, drawn to an antibody, classified in class 530, subclass 387.1.

Claims 1-31 are cancelled and new claims 32-36, directed to subject matter of cancelled claims 27-31, are introduced herein.

If it is believed that a telephone conversation with Applicants' attorney would be helpful in expediting prosecution of this, the subject application, the Examiner is invited to call the undersigned.

Respectfully submitted,

Date: June 23, 1999

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SPECIFICATION

NOVEL PROTEINS AND METHODS FOR PRODUCING THE PROTEINS

Field of the invention

This invention relates to a novel protein, osteoclastogenesis inhibitory factor (OCIF), and methods for producing the protein.

Background of the invention

Human bones are always remodelling by the repeated process of resorption and reconstitution. In the process, osteoblasts and osteoclasts are considered to be the cells mainly responsible for bone formation and bone resorption, respectively. A typical example of disease caused by the progression of abnormal bone metabolism is osteoporosis. The disease is known to be provoked by the condition in which bone resorption by osteoclasts exceeds bone formation by osteoblasts, but the mechanism of osteoporosis has not yet been completely elucidated. Osteoporosis causes pain in the bone and makes the bone fragile, leading to fracture. Since osteoporosis increases the number of bedridden old people, it has become a social issue with the increasing number of old people. Therefore, efficacious drugs for the treatment of the disease are expected to be developed. Bone mass reduction caused by the abnormal bone metabolism is thought to be prevented by inhibiting bone resorption, improving bone formation, or improving the balanced metabolism.

Bone formation is expected to be promoted by stimulating growth, differentiation, or activation of osteoblasts. Many cytokines are reported to stimulate growth or differentation of osteoblasts , i.e. fibroblast growth

factor (FGF) (Rodan S.B. et al., Endocrinology vol. 121, p1917, 1987), insulin-like growth factor-I (IGF-I) (Hock J.M. et al., Endocrinology vol. 122, p254, 1988), insulin-like growth factor-II (IGF-II) (McCarthy T. et al., Endocrinology vol. 124, p301, 1989), Activin A (Centrella M. et al., Mol, Cell, Biol. vol. 11, p250, 1991), Vasculotropin (Varonique M et al., Biochem. Biophys. Res. Commun. vol. 199, p380, 1994), and bone morphogenetic protein (BMP) (Yamaguchi, A et al., J. Cell Biol. vol. 113, p682, 1991, Sampath T.K. et al., J. Biol Chem. vol. 267, p20532, 1992, and Knutsen R. et al., Biochem. Biophys. Res. Commun. vol. 194, p1352, 1993.

On the other hand, cytokines which inhibits differentiation and/or maturation of osteoclasts have been paid attention and have been intensively studied. Transforming growth factor-β (Chenu C. et al., Proc. Natl. Acad. Sci. USA, vol. 85, p5683, 1988) and interleukin-4 (Kasano K. et al., Bone-Miner., vol. 21, p179, 1993) are found to inhibit the differentiation of osteoclasts. Calcitonin (Bone-Miner., vol. 17, p347, 1992), Macrophage colony-stimulating factor (Hattersley G. et al. J. Cell. Physiol. vol. 137, p199, 1988), interleukin-4 (Watanabe, K. et al., Biochem. Biophys. Res. Commun. vol. 172, p1035, 1990), and interferon-γ (Gowen M. et al., J. Bone Miner. Res., vol. 1, p469, 1986) are found to inhibit bone resorption by osteoclasts.

These cytokines are expected to be efficacious drugs for improving bone mass reduction by stimulating bone formation and/or by inhibiting bone resorption. The cytokines such as insulin like growth factor-I and bone morphogenetic proteins are now investigated in clinical trials for their

effects in treatment of patients with bone diseases. Calcitonin is already used as a drug to care osteoporosis and to diminish pain in osteoporosis.

Examples of drugs now clinically utilized for the treatment of bone diseases and for shortening the treatment period are dihydroxyvitamine D_3, vitamin K_2, calcitonin and its derivatives, hormones such as estradiol, ipriflavon, and calcium preparations . However, these drugs do not provide satisfactory therapeutic effects, and novel drug substances have been expected to be developed. As mentioned, bone metabolism is controlled in the balance between bone resorption and bone formation. Therefore, cytokines which inhibit osteoclast differentiation and/or maturation are expected to be developed as drugs for the treatment of bone diseases such as osteoporosis.

Disclosure of Invention

This invention was initiated from the view point described above. The purpose of this invention is to offer both a novel factor termed osteoclastogenesis inhibitory factor (OCIF) and a procedure to produce the factor efficiently.

The inventors have intensively searched for osteoclastogenesis inhibitory factors in human embryonic fibloblast IMR-90 (ATCC CCL186) conditioned medium and have found a novel osteoclastogenesis inhibitory factor (OCIF) which inhibits differentiation and/or maturation of osteoclasts.

The inventors have established a method for accumulating the protein to a high concentration by culturing IMR-90 cells using alumina ceramic pieces as the cell adherence matrices.

The inventors have also established an efficient method for isolating the protein, OCIF, from the IMR-90 conditioned medium using the following sequential column chromatography, ion-exchange, heparin affinity, cibacron-blue affinity, and reverse phase.

The inventors, based on the amino acid sequence of the purified natural OCIF, successfully cloned a cDNA encoding this protein. The inventors established also a procedure to produce this protein which inhibits differentiation of osteoclasts. This invention concerns a protein which is produced by human lung fibroblast cells, has molecular weights in SDS-PAGE of 60 KD in the reducing conditions and 120 KD under the non-reducing conditions, has affinity for both cation-exchange resins and heparin, reduces its activity to inhibit differentiation and maturation of osteoclasts if treated for 10 minutes at 70 ℃ or for 30 minutes at 56 ℃, and lose its activity to inhibit differentiation and maturation of osteoclasts by the treatment for 10 minutes at 90 ℃. The amino acid sequence of the protein OCIF which is described in the present invention is clearly different from any of know factors inhibiting formation of osteoclasts.

The invention includes a method to purify OCIF protein, comprising ; (1) culturing human fibroblasts, (2) applying the conditioned medium to a heparin column to obtain the adsorbed fraction, (3) purifying the OCIF protein using a cation-exchange column, (4) purifying the OCIF protein using a heparin affinity column, (5) purifying the OCIF protein using a cibacron blue affinity column, (6) isolating the OCIF protein using reverse-phase column chromatography. Cibacron blue F3GA coupled to a carrier made of synthetic

hydrophilic polymers is an example of materials used to prepare Cibacron blue columns. These columns are conventionally called "blue colomns".

The invention includes a method for accumulating the OCIF protein to a high concentration by culturing human fibroblasts using alumina ceramic pieces as the cell-adherence matrices.

Moreover, the inventors determined the amino acid sequences of the peptides derived from OCIF, designed the primers based on these amino acid sequences, and obtained cDNA fragments encoding OCIF from a cDNA library of IMR-90 cells.

Detailed description of the invention

The OCIF protein of the present invention can be isolated from human fibroblast conditioned medium with high yield. The procedure to isolate OCIF is based on ordinary techniques for purifying proteins from biomaterials, in accordance with the physical and chemical properties of OCIF protein. For example, concentrating procedure includes ordinary biochemical techniques such as ultrafiltration, lyophylization, and dialysis. Purifying procedure includes combinations of several chromatographic techniques for purifying proteins such as ion-exchange column chromatography, affinity column chromatography, gel filtration column chromatography, hydrophobic column chromatography, reverse phase column chromatography, and preparative gel electrophoresis. The human fibroblast used for production of the OCIF protein is preferably IMR-90. A method for producing the IMR-90 conditioned medium is preferably a process comprising, adhering human embryonic fibroblast IMR-90 cells to alumina

ceramic pieces in roller-bottles, using DMEM medium supplemented with 5 % new born calf serum for the cell culture, and cultivating the cells in roller-bottles for 7 to 10 days by stand cultivation. CHAPS (3-[(3-cholamid opropyl)-dimethylammonio]-1-propanesulfonate) is prefarably added to the buffer as a detergent in the purification steps of OCIF protein.

OCIF protein of the instant invention can be initially obtained as a heparin binding basic OCIF fraction by applying the culture medium to a heparin column (Heparin-Sepharose CL-6B, Pharmacia), eluting with 10 mM Tris-HCl buffer, pH 7.5, containing 2 M NaCl, and then by applying the OCIF fraction to a Q • anion-exchange column (HiLoad-Q/FF, Pharmacia), and collecting non-adsorbed fraction. OCIF protein can be purified by subjecting the obtained OCIF fraction to purification on a S • cation-exchange column (HiLoad-S/FF, Pharmacia). a heparin column (Heparin-5PW, TOSOH), Cibacrone Blue column (Blue-5PW, TOSOH), and a reverse-phase column (BU-300 C4, Perkin Elmer) and the material is defined by the previously described properties.

The present invention relates to a method of cloning cDNA encoding the OCIF protein based on the amino acid sequence of natural OCIF and a method of obtaining recombinant OCIF protein that inhibits differentiation and/or maturation of osteoclasts. The OCIF protein is purified according to the method described in the present invention and is treated with endopeptidase (for example, lysylendopeptidase). The amino acid sequences of the peptides produced by the digestion are determined and the mixture of oligonucleotides

that can encode each internal amino acid sequence was systhesized. The OCIF cDNA fragment is obtained by PCR (preferably RT-PCR, reverse transcriptase PCR) using the oligonucleotide mixtures described above as primers. The full length OCIF cDNA encoding the OCIF protein is cloned from a cDNA library using the obtained OCIF DNA fragment as a probe. The OCIF cDNA containing the entire coding region is inserted into an expression vector. The recombinant OCIF can be produced by expressing the OCIF cDNA containing the entire coding region in mammalian cells or bacteria.

The present invention relates to the novel proteins OCIF2, OCIF3, OCIF4, and OCIF5 that are variants of OCIF and have the activity described above. These OCIF variants are obtained from the cDNA library constructed with IMR-90 poly(A) + RNA by hybridization using the OCIF cDNA fragment as a probe. Each of the OCIF variant cDNAs containing the entire coding region is inserted into an expression vector. Each recombinant OCIF variant can be produced by expressing each of the OCIF variant cDNAs containing the entire coding region in the conventional hosts. Each recombinant OCIF variant can be purified according to the method described in this invention. Each recombinant OCIF variant has an ability to inhibit osteoclastogenesis.

The present invention further includes OCIF mutants. They are substitution mutants comprising replacement of one cysteine residue possibly involved in dimer formation with serine residue, and various deletion mutants of OCIF. Substitutions or deletions are introduced into the OCIF cDNA using

polymerase chain reaction (PCR) or by restriction enzyme digestion. Each of these mutated OCIF cDNAs is inserted into a vector containing an appropriate promoter for gene expression. The resultant expression vector for each of the OCIF mutants is transfected into eukaryotic cells such as mammalian cells. Each of OCIF mutants can be obtained and purified from the conditioned media of the transfected cells.

The present invention provides polyclonal antibodies and a method to quantitatively determine OCIF concentration using these polyclonal antibodies.

As antigens (immunogens), natural OCIF obtained from IMR-90 conditioned medium, recombinant OCIF produced by such hosts as microorganisms and eukaryotes using OCIF cDNA, synthetic peptides designed based on the amino acid sequence of OCIF, or peptides obtained from OCIF by partial digestion can be used. Anti-OCIF polyclonal antibodies are obtained by immunizing appropriate mammals with the antigens in combination with adjuvants for immunization if necessary, purifying from the serum by the ordinary purification methods. The anti-OCIF polyclonal antibodies which are labelled with rasioisotopes or enzymes can be used in radio-immunoassay (RIA) system or immunoassay (EIA) system. By using these assay systems, the concentrations of OCIF in biological materials such as blood and ascites and cells-culture medium can be easily determined.

The antibodies in the present invention can be used in radio immunoassay (RIA) or enzyme immunoassay (EIA). By using these assay systems, the concentration of OCIF in biological materials such as blood and ascites can

be easily determined.

The present invention provides novel monoclonal antibodies and a method to quantitatively determine OCIF concentration using these monoclonal antibodies.

Anti-OCIF monoclonal antibodies can be produced by the conventional method using OCIF as an antigen. Native OCIF obtained from the culture medium of IMR-90 cells and recombinant OCIF produced by such hosts as microorganisms and eukaryotes using OCIF cDNA can be used as antigens. Alternatively, synthesized peptides designed based on the amino acid sequence of OCIF and peptides obtained from OCIF by partial digestion can be also used as antigens. Immunized lymphocytes obtained by immunization of mammals with the antigen or by an in vitro immunization method were fused with myeloma of mammals to obtain hybridoma. The hybridoma clones secreting antibody which recognizes OCIF were selected from the hybridomas obtained by the cell fusion. The desired antibodies can be obtained by cell culture of the selected hybridoma clones. In preparation of hybridoma, small animals such as mice or rats are generally used for immunization. To immunize, OCIF is suitably diluted with a saline solution (0.15 M NaCl), and is intravenously or intraperitoneally administered with an adjuvant to animals for 2 -5 times every 2 -20 days. The immunized animal was killed three days after final immunization, the spleen was taken out and the splenocytes were used as immunized B lymphocytes.

Mouse myeloma cell lines for cell fusion with the immunized B lymphocytes include, for example, p3/x63-Ag8, p3-U1, NS-1, MPC-11, SP-2/0, FO, p3x63

Ag8.653, and S194. Rat R-210 cell line may also be used. Human B lymphocytes are immunized by an in vitro immunization method and are fused with human myeloma cell line or EB virus transformed human B lymphocytes which are used as a parent cell line for cell fusion, to produce human type antibody.

Cell fusion of the immunized B lymphocytes and myeloma cell line is carried out principally by the conventional methods. For example, the method of Koehler G. et al. (Nature 256, 495-497, 1975) is generally used, and also an electric pulse method can be applied to cell fusion. The immunized B lymphocytes and transformed B cells are mixed at conventional ratios and a cell culture medium without FBS containing polyethylene glycol is generally used for cell fusion. The B lymphocytes fused with myeloma cell lines are cultured in HAT selection medium containing FBS to select hybridoma.

For screening of hybridoma producing anti-OCIF antibody, EIA, plaque assay, Ouchterlony, or agglutination assay can be principally used. Among them, EIA is simple and easy to operate with sufficient accuracy and is generally used. By EIA using purified OCIF, the desired antibody can be selected easily and accurately. Thus obtained hybridoma can be cultured by the conventional method of cell culture and frozen for stock if necessary. The antibody can be produced by culturing hybridoma using the ordinary cell culture method or by transplanting hybridoma intraperitoneally to animals. The antibody can be purified by the ordinary purification methods such as salt precipitation, gel filtration, and affinity chromatography. The obtained antibody specifically reacts with OCIF and can be used for determination of OCIF concentration and for purification of OCIF. The antibodies of the

present invention recognize epitopes of OCIF and have high affinity to OCIF. Therefore, they can be used for the construction of EIA. By (using) this assay system, the concentration of OCIF in biological materials such as blood and ascites can be easily determined.

The agents used for treating bone diseases that contain OCIF as an effective ingredient are provided by the present invention. Rats were subjected to denervation of left forelimb. Test compounds were administered daily after surgery for 14 days. After 2 weeks treatment, the animals were sacrificed and their forelimbs were dissected. Thereafter bones were tested for mechanical strength by three point bending method. OCIF improved mechanical strength of bone in a dose dependent manner.

The OCIF protein of the invention is useful as a pharmaceutical ingredients for treating or improving decreased bone mass in such as osteoporosis, bone diseases such as rheumatism, osteoarthritis, and abnormal bone metabolism in multiple myeloma. The OCIF protein is also useful as an antigen to establish immunological diagnosis of the diseases. Pharmaceutical preparations containing the OCIF protein as an active ingredients are formulated and can be orally or parenterally administered. The preparation contains the OCIF protein of the present invention as an efficacious ingredient and is safely administered to human and animals. Examples of the pharmaceutical preparations include compositions for injection or intravenous drip, suppositories, nasal preparations, sublingual preparations, and tapes for percutaneous absorption. The pharmaceutical preparation for injection can

be prepared by mixing the pharmacologically efficacious amount of OCIF protein and pharmaceutically acceptable carriers. The carriers are vehicles and/or activators, e.g. amino acids, saccharides, cellulose derivatives, and other organic and inorganic compounds which are generally added to active ingredients. When the OCIF protein is mixed with the vehicles and/or activators to prepare injections, pH adjuster, buffer, stabilizer, solubilizing agent, etc. can be added, if necessary.

Brief description of the figures

Figure 1 shows the elution pattern of crude OCIF protein (Hiload-Q/FF pass-through fraction ; sample 3) from a Hiload-S/HP column.

Figure 2 shows the elution pattern of crude OCIF protein (heparin-5PW fraction ; sample 5) from a blue-5PW column.

Figure 3 shows the elution pattern of OCIF protein (blue-5PW fraction 49 to 50) from a reverse-phase column.

Figure 4 shows the SDS-PAGE of isolated OCIF proteins under reducing conditions or non-reducing conditions.

Description of the lanes,

lane 1,4 ; molecular weight marker proteins

lane 2,5 ; OCIF protein of peak 6 in figure 3

lane 3,6 ; OCIF protein of peak 7 in figure 3

Figure 5 shows the elution pattern of peptides obtained by the digestion of pyridyl ethylated OCIF protein digested with lysylendopeptidase, on a reverse-phase column.

Figure 6 shows the SDS-PAGE of isolated natural(n) OCIF protein and recombinant(r) OCIF proteins under non-reducing conditions. rOCIF(E) and rOCIF(C) were produced in 293/EBNA cells and in CHO cells, respectively.

Description of the lanes,

lane 1 ; molecular weight marker proteins

lane 2 ; a monomer type nOCIF protein

lane 3 ; a dimer type nOCIF protein

lane 4 ; a monomer type rOCIF(E) protein

lane 5 ; a dimer type rOCIF(E) protein

lane 6 ; a monomer type rOCIF(C) protein

lane 7 ; a dimer type rOCIF(C) protein

Figure 7 shows the SDS-PAGE of isolated natural(n) OCIF proteins and recombinant (r) OCIF proteins under reducing conditions. rOCIF(E) and rOCIF(C) were produced in 293/EBNA cells and in CHO cells, respectively.

Description of the lanes,

lane 8 ; molecular weight marker proteins

lane 9 ; a monomer type nOCIF protein

lane 10 ; a dimer type nOCIF protein

lane 11 ; a monomer type rOCIF(E) protein

lane 12 ; a dimer type rOCIF(E) protein

lane 13 ; a monomer type rOCIF(C) protein

lane 14 ; a dimer type rOCIF(C) protein

Figure 8 shows the SDS-PAGE of isolated natural(n) OCIF proteins and recombinant(r) OCIF proteins from which N-linked sugar chains were removed

under reducing conditions. rOCIF(E) and rOCIF(C) are rOCIF protein produced in 293/EBNA cells and in CHO cells, respectively.

Description of the lanes,

lane 15 ; molecular weight marker proteins

lane 16 ; a monomer type nOCIF protein

lane 17 ; a dimer type nOCIF protein

lane 18 ; a monomer type rOCIF(E) protein

lane 19 ; a dimer type rOCIF(E) protein

lane 20 ; a monomer type rOCIF(C) protein

lane 21 ; a dimer type rOCIF(C) protein

Figure 9 shows comparison of amino acid sequences between OCIF and OCIF2.

Figure 10 shows comparison of amino acid sequences between OCIF and OCIF3.

Figure 11 shows comparison of amino acid sequences between OCIF and OCIF4.

Figure 12 shows comparison of amino acid sequences between OCIF and OCIF5.

Figure 13 shows standard curve for determination of OCIF protein concentration by an EIA employing anti-OCIF polyclonal antibodies.

Figure 14 shows standard curve for determination of OCIF protein concentration by an EIA employing anti-OCIF monoclonal antibodies.

Figure 15 shows the effect of rOCIF protein on osteoporosis.

Best Mode for Carrying Out the Invention

The present invention will be further explained by the following examples, however, the scope of the invention is not restricted to the examples.

EXAMPLE 1

Preparation of a conditioned medium of human fibroblast IMR-90

Human fetal lung fibroblast IMR-90 (ATCC-CCL186) cells were cultured on alumina ceramic pieces (80 g) (alumina: 99.5%, manufactured by Toshiba Ceramic K.K.) in DMEM medium (manufactured by Gibco BRL Co.) supplemented with 5% CS and 10mM HEPES buffer (500 ml/roller bottle) at 37℃ under the presence of 5% CO_2 for 7 to 10 days using 60 roller bottles (490 cm^2, 110 x 171mm, manufactured by Coning Co.)in static culture. The conditioned medium was harvested, and a fresh medium was added to the roller bottles. About 30L of IMR-90 conditioned medium per batch culture was obtained. The conditioned medium was designated as sample 1.

EXAMPLE 2

Assay method for osteoclast development inhibitory activity

Osteoclast development inhibitory activity was assayed by measuring tartrate-resistant acid phosphatase(TRAP) activity according to the methods of M. Kumegawa et.al (Protein ・Nucleic Acid・Enzyme, vol.34 p999,1989) and N. Takahashi et.al (Endocrynology, vol.122, p1373, 1988) with modifications. Briefly, bone marrow cells obtained from 17 day-old mouse were suspended in α-MEM (manufactured by GIBCO BRL Co.) containing 10% FBS, $2x10^{-8}$M of activated vitamin D_3, and each test sample, and were inoculated to each well of 96-well plate at a cell density of $3x10^5$ cells/0.2 ml/well. The plates were incubated for 7 days at 37℃ in humidified 5%CO_2. Cultures were further continued by replacing 0.16 ml of old medium with the same volume of fresh

medium on day 3 and day 5 after starting cultivation. On day 7, after washing the plates with phosphate buffered saline, cells were fixed with ethanol/acetone (1:1) for 1 min. at room temperature, and then osteoclast development was tested by determining for phosphatase activity using a kit (Acid Phosphatase, Leucocyte, Catalog No. 387-A, manufactured by Sigma Co.). The decrease of TRAP positive cells was taken as an indication of OCIF activity.

EXAMPLE 3

Purification of OCIF

i) Heparin Sepharose CL-6B column chromatography

The 90L of IMR-90 conditioned medium (sample 1) was filtrated with 0.22 μ membrane filter (hydrophilic Milidisk, 2000 cm^2, Milipore Co.), and was divided into three portions. Each portion (30 l) was applied to a heparin Sepharose CL-6B column (5 x 4.1 cm, Pharmacia Co.) equilibrated with 10mM Tris-HCl containing 0.3M NaCl, pH 7.5. After washing the column with 10mM Tris-HCl, pH 7.5 at a flow rate of 500 ml/hr., heparin Sepharose CL-6B adsorbent protein fraction was eluted with 10mM Tris-HCl, pH 7.5, containing 2M NaCl. The fraction was designated as sample 2.

ii) HiLoad-Q/FF column chromatography

The heparin Sepharose-adsorbent fraction (sample 2) was dialyzed against 10mM Tris-HCl, pH 7.5, supplemented with CHAPS to a final concentration of 0.1%, incubated at 4 ℃ overnight, and divided into two portions. Each

portion was then applied to an anion-exchange column (HiLoad-Q/FF, 2.6 x 10 cm, Pharmacia Co.) which was equilibrated with 50mM Tris-HCl, 0.1% CHAPS, pH 7.5 to obtain a non-adsorbent fraction (1000 ml). The fraction was designated as sample 3.

iii) HiLoad-S/HP column chromatography

The HiLoad-Q non-adsorbent fraction (sample 3) was applied to a cation-exchange column (HiLoad-S/HP, 2.6 x 10 cm, Pharmacia Co.) which was equilibrated with 50 mM Tris-HCl, 0.1% CHAPS, pH 7.5. After washing the column with 50 mM Tris-HCl, 0.1% CHAPS, pH 7.5, the adsorbed protein was eluted with linear gradient from 0 to 1 M NaCl at a flow rate of 8 ml/min for 100 min. and fractions (12 ml) were collected. Each ten fractions from number 1 to 40 was pooled to form one portion. Each 100 μl of the four portions was tested for OCIF activity. OCIF activity was observed in fractions from 11 to 30 (as shown in Figure 1). The fractions from 21 to 30 which had higher specific activity were collected and was designated as sample 4.

iv) Heparin-5PW affinity column chromatography

One hundred and twenty ml of HiLoad-S fraction from 21 to 30 (sample 4) was diluted with 240 ml of 50 mM Tris-HCl, 0.1% CHAPS, pH 7.5, and applied to heparin-5PW affinity column (0.8 x 7.5 cm, Tosoh Co.) which was equilibrated with 50mM Tris-HCl, 0.1% CHAPS, pH 7.5. After washing the column with 50mM Tris-HCl, 0.1% CHAPS, pH 7.5, the adsorbed protein was eluted with linear gradient from 0 to 2M NaCl at a flow rate of 0.5ml/min for 60 min. and fractions

(0.5 ml) were collected. Fifty μl was removed from each fraction to test for OCIF activity. The active fractions, eluted with 0.7 to 1.3M NaCl was pooled and was designated as sample 5.

v) Blue 5PW affinity column chromatography

Ten ml of sample 5 was diluted with 190 ml of 50mM Tris-HCl, 0.1% CHAPS, pH 7.5 and applied to a blue-5PW affinity column, (0.5x5 cm, Tosoh Co.) which was equilibrated with 50mM Tris-HCl, 0.1% CHAPS, pH 7.5. After washing the column with 50mM Tris-HCl, 0.1% CHAPS, pH7.5, the adsorbed protein was eluted with a 30 ml linear gradient from 0 to 2M NaCl at a flow rate of 0.5 ml/min., and fractions (0.5 ml) were collected. Using 25 μl of each fraction, OCIF activity was evaluated. The fractions number 49 to 70, eluted with 1.0-1.6M NaCl had OCIF activity.

vi) Reverse phase column chromatography

The blue 5PW fraction obtained by collecting fractions from 49 to 50 was acidified with 10μl of 25% TFA and applied to a reverse phase C4 column (BU-300, 2.1x220mm, manufactured by Perkin-Elmer) which was equilibrated with 0.1% of TFA and 25% of acetonitrile. The adsorbed protein was eluted with linear gradient from 25 to 55% acetonitrile at a flow rate of 0.2 ml/min. for 60 min., and each protein peak was collected (Fig.3). One hundred μl of each peak fraction was tested for OCIF activity, and peak 6 and the peak 7 had OCIF activity. The result was shown in Table 1.

Table 1

OCIF activity eluted from reverse phase C4 column

Sample	Dilution			
	1/40	1/120	1/360	1/1080
Peak 6	++	++	+	-
Peak 7	++	+	-	-

[++ means OCIF activity inhibiting osteoclast development more than 80%, + means OCIF activity inhibiting osteoclast development between 30% and 80%, and - means no OCIF activity.]

EXAMPLE 4

Molecular weight of OCIF protein

The two protein peaks (6 and 7) with OCIF activity were subjected to SDS-polyacrylamide gel electrophoresis under reducing and non-reducing conditions. Briefly, 20 μl of each peak fraction was concentrated under vacuum and dissolved in 1.5 μl of 10mM Tris-HCl, pH 8, 1mM EDTA, 2.5% SDS, 0.01% bromophenol blue, and incubated at 37℃ overnight under non-reducing conditions or under reducing conditions (with 5% of 2-mercaptoethanol). Each 1.0 μl of sample was then analyzed by SDS-polyacrylamide gel electrophoresis with a gradient gel of 10-15% acrylamide (Pharmacia Co.) and an electrophoresis-device (Fast System, Pharmacia Co.). The following molecular weight marker proteins were used to calculate molecular weight : phosphorylase b (94 kD), bovine serum albumin (67 kD), ovalbumin (43 kD), carbonic anhydrase (30 kD), trypsin inhibitor (20.0 kD), and lactalbumin (14.4 kD). After

electrophoresis, protein bands were visualized by silver stain using Phast Silver Stain Kit. The results were shown in Fig. 4.

A protein band with an apparent 60 KD was detected in the peak 6 protein under both reducing and non-reducing conditions. A protein band with an apparent 60 KD was detected under reducing conditions and a protein band with an apparent 120 KD was detected under non-reducing conditions in the peak 7 protein. Therefore, the protein of peak 7 was considered to be a homodimer of the protein of peak 6.

EXAMPLE 5

Thermostability of OCIF

Twenty μl of sample from the blue-5PW fractions 51 and 52 was diluted to 30μl with 10 mM phosphate buffered saline, pH 7.2, and incubated for 10 min. at 70℃ or 90 ℃, or for 30 min. at 56℃. The heat-treated samples were tested for OCIF activity. The results were shown in Table 2.

Table 2

Thermostability of OCIF

Sample	Dilution		
	1/300	1/900	1/2700
untreated	++	+	-
70℃, 10 min	+	-	-
56℃, 30 min	+	-	-
90℃, 10 min	-	-	-

[++ means OCIF activity inhibiting osteoclast development more than 80%, +means OCIF activity inhibiting osteoclast development between 30% and 80%, and - means no OCIF activity.]

EXAMPLE 6

Internal amino acid sequence of OCIF protein

Each 2 fractions (1 ml) from No. 51-70 of blue-5PW fraction was acidified with 10 μl of 25% TFA, and was applied to a reverse phase C4 column (BU-300, 2.1x220mm, manufactured by Perkin-Elmer Co.) equilibrated with 25% of acetonitrile containing 0.1 % TFA. The adsorbed protein was eluted with a 12 ml linear gradient of 25 to 55% acetonitrile at a flow rate of 0.2 ml/min, and the protein fractions corresponding to peak 6 and peak 7 were collected, respectively. The protein of each peak was applied to a protein sequencer (PROCISE 494, Perkin-Elmer Co.). However, the N-terminal sequence of the protein of each peak could not be analyzed. Therefore, N-terminal of the protein of each peak was considered to be blocked. So, internal amino acid sequences of these proteins were analyzed.

The protein of peak 6 or peak 7 purified by C4-HPLC was concentrated by centrifugation and pyridilethylated under reducing conditions. Briefly, 50 μl of 0.5 M Tris-HCl, pH 8.5, containing 100 μg of dithiothreitol, 10mM EDTA, 7 M guanidine-HCl, and 1% CHAPS was added to each samples, and the mixture was incubated overnight in the dark at a room temperature. Each the mixture was acidified with 25% TFA (a final concentration 0.1%) and was applied to a reversed phase C4 column (BU-300, 2.1x30mm, Perkin-Elmer Co.) equilibrated with 20 % acetonitrile containing 0.1 % TFA. The pyridil-ethylated OCIF

protein was eluted with a 9 ml linear gradient from 20 to 50% acetonitrile at a flow rate of 0.3 ml/min, and each protein peak was collected. The pyridil-ethyrated OCIF protein was concentrated under vacuum , and dissolved in 25μl of 0.1 M Tris-HCl, pH 9, containing 8 M Urea, and 0.1 % Tween 80. Seventy three μl of 0.1 M Tris-HCl, pH 9, and 0.02 μg of lysyl endopeptidase (Wako Pure Chemical, Japan) were added to the tube, and incubated at 37 ℃ for 15 hours. Each digest was acidified with 1 μl of 25% TFA and was applied to a reverse phase C8 column (RP-300, 2.1x220mm, Perkin-Elmer Co.) equilibrated with 0.1% TFA.

The peptide fragments were eluted from the column with linear gradient from 0 to 50 % acetonitrile at a flow rate of 0.2 ml/min for 70 min., and each peptide peak was collected. Each peptide fragment (P1 - P3) was applied to the protein sequencer. The sequences of the peptides were shown in Sequence Numbers 1 - 3, respectively.

EXAMPLE 7

Determination of nucleotide sequence of the OCIF cDNA

i) Isolation of poly(A) + RNA from IMR-90 cells

About 10 ug of poly(A) + RNA was isolated from $1x10^8$ cells of IMR-90 by using Fast Track mRNA isolation kit (Invitrogen) according to the manufacturer's instructions.

ii) Preparation of mixed primers

The following two mixed primers were synthesized based on the amino acid

sequences of two peptides (peptide P2 and peptide P3, sequence numbers 2 and 3, respectively). All the oligonucleotides in the mixed primers No. 2F can code for the amino acid sequence from the sixth residue, glutamine (Gln) to the twelfth residue, leucine (Leu), in peptide P2. All the oligonucleotides in the mixed primers No. 3R can code for the amino acid sequence from the sixth residue, histidine (His), to the twelfth residue, lysine (Lys), in peptide P3. The sequences of the mixed primers No. 2F and No. 3R were shown in Table 3.

Table 3

No. 2F

```
5'-CAAGAACAAA CTTTTCAATT-3'
    G  G  G   C  C  GC
              A
              G
```

No. 3R

```
5'-TTTATACATT GTAAAAGAAT G-3'
  C  G     C   G  GCTG
           A      C
           G      T
```

iii) Amplification of OCIF cDNA fragment by PCR (Polymerase chain reaction)

First strand cDNA was generated using Superscript II cDNA synthesis kit

(Gibco BRL) and 1 ug of poly(A) + RNA obtained in the example 7-i) according to the manufacturer's instructions. The DNA fragment encoding OCIF was obtained by PCR using the cDNA template and the primers shown in EXAMPLE 7-ii).

PCR was performed with the conditions as follows;

10X Ex Taq Buffer (Takara Shuzo)	5	ul
2.5 mM solution of dNTPs	4	ul
cDNA solution	1	ul
Ex Taq (Takara Shuzo)	0.25	ul
sterile distilled water	29.75	ul
40 uM solution of primers No. 2F	5	ul
40 uM solution of primers No. 3R	5	ul

The components of the reaction were mixed in a microcentrifuge tube. An initial denaturation step at 95 ℃ for 3 min was followed by 30 cycles of denaturation at 95℃ for 30 sec annealing at 50 ℃ for 30 sec and extention at 70 ℃ for 2min. After the amplification, final extention step was performed at 70 ℃ for 5min. The size of PCR products were determined on a 1.5 % agarose gel electrophoresis. About 400 bp OCIF DNA fragment was obtained.

EXAMPLE 8

Cloning of the OCIF cDNA fragment amplified by PCR and determination of its DNA sequence

The OCIF cDNA fragment amplified by PCR in EXAMPLE 7-iii) was inserted in the plasmid, pBluescript II SK⁻ using DNA ligation kit ver. 2 (Takara Shuzo) according to the method by Marchuk, D. et al. (Nucleic Acids Res., vol 19, p1154, 1991). E.coli. DH5 α (Gibco BRL) was transformed with ligation mixture. The transformants were grown and a plasmid containing the OCIF cDNA (about 400 bp) was purified using the commonly used method. This plasmid was called pBSOCIF. The sequence of OCIF cDNA in pBSOCIF was determined using Taq Dye Deoxy Terminater Cycle Sequencing kit (Perkin Elmer). The size of the OCIF cDNA is 397 bp. The OCIF cDNA encodes an amino acid sequence containing 132 residues. The amino acid sequences of the internal peptides (peptide P2 and peptide P3, sequence number 2 and 3, respectively) that were used to design the primers were found at N- or C- terninal side in the amino acid sequence of the 132 amino acid polypeptide predicted by the 397 bp OCIF cDNA. In addition, the amino acid sequence of the internal peptide P1 (sequence number 1) was also found in the predicted amino acid sequence of the polypeptide. These data show that the 397 bp OCIF cDNA is a portion of the full length OCIF cDNA.

EXAMPLE 9

Preparation of the DNA probe

The 397 bp OCIF cDNA was prepared according to the conditions described in EXAMPLE 7-iii). The OCIF cDNA was subjected to a preparative agarose gel electrophoresis. The OCIF cDNA was purified from the gel using QIAEX gel extraction kit (QIAGEN), labeled with [α^{32}P]dCTP using Megaprime DNA labeling

system (Amersham) and used to select a phage containing the full length OCIF cDNA.

EXAMPLE 10

Preparation of the cDNA library

cDNA was generated using Great Lengths cDNA synthesis kit (Clontech), oligo (dT) primer, [α^{32}P]dCTP and 2.5 ug of poly(A) + RNA obtained in the example 7-i) according to the manufacturer's instructions. EcoRI-SalI-NotI adaptor was ligated to the cDNA. The cDNA was separated from the free adaptor and unincorporated free [α^{32}P]dCTP. The purified cDNA was precipitated with ethanol and dissolved in 10 ul of TE buffer (10 mMTris-HCl (pH8.0), 1 mM EDTA). The cDNA with the adaptor was inserted in λZAP EXPRESS vector (Stratagene) at EcoRI site. The recombinant λZAP EXPRESS phage DNA containing the cDNA was in vitro packaged using Gigapack gold II packaging extract (Stratagene) and recombinant λZAP EXPRESS phage library was prepared.

EXAMPLE 11

Screening of recombinant phage

Recombinant phages obtained in EXAMPLE 10 were infected to E. Coli, XL1-Blue MRF' (Stratagene) at 37 ℃ for 15 min.. The infected E.coli cells were added to NZY medium containing 0.7 % agar at 50℃ and plated on the NZY agar plates. After the plates were incubated at 37 ℃ overnight, Hybond N (Amersham) were placed on the surface of plates containing plaques. The membranes were denatured in the alkali solution, neutralized, and washed in

2xSSC according to the standard protocol. The phage DNA was immobilized on the membranes using UV Crosslink (Stratagene). The membranes were incubated in the hybridization buffer (Amersham) containing 100 μg/ml salmon sperm DNA at 65℃ for 4 hours and then incubated at 65 ℃ overnight in the same buffer containing $2x10^5$ cpm/ml denatured OCIF DNA probe. The membranes were washed twice with 2xSSC and twice with a solution containing 0.1xSSC and 0.1 % SDS at 65 ℃ for 10 min each time. The positive clones were purified by repeating the screening twice. The purified λZAP EXPRESS phage clone containing about 1.6 kb DNA insert was used in the experiments described below. This phage was called λOCIF. The purified λOCIF and the infected into E. Coli XL1-Blue MRF' (Stratagene) according to a protocol of λZAP EXPRESS cloning kit (Stratagene). The culture broth of infected XL1-Blue MRF' was prepared.

Purified 1OCIF and ExAssist helper phage (Stratagene) were co-infected into E. coli strain XL-1 blue MRF' according to the protocol supplied with the kit. The culture broth of the co-infected XL-1 blue MRF' was added to a culture of E. coli strain XLOR (Stratagene) to transform them. Thus we obtained a Kanamycin-resistant transformant harboring a plasmid designated pBKOCIF which is a pBKCMV (Stratagene) vector containing the 1.6 kb insert fragment.

The transformant including the plasmid containing about 1.6 kb OCIF cDNA was obtained by picking up the kanamycin-resistant colonies. The plasmid was called pBKOCIF. The transformant has been deposited to National Institute of Bioscience and Human-Technology (NIBH), Agency of Industrial Science and Tecnology as "FERM BP-5267" as pBK/O1F10. A national deposit (Accession number, FERM P-14998) was transfered to the international deposit, on October 25, 1995

according to the Budapest treaty. The transformant pBK/OIF10 was grown and the plasmid pBKOCIF was purified according to the standard protocol.

EXAMPLE 12

Determination of the nucleotide sequence of OCIF cDNA containing the full coding region.

The nucleotide sequence of OCIF cDNA obtained in EXAMPLE 11 was determined using Taq Dye Deoxy Terminater Cycle Sequencing kit (Perkin Elmer). The primers used were T3, T7 primers (Stratagene) and synthetic primers designed according to the OCIF cDNA sequence. The sequences of these primers are shown in sequence numbers 16 to 29. The nucleotide sequence of the OCIF cDNA is shown in sequence number 6 and the amino acid sequence predicted by the cDNA sequence is shown in sequence number 5.

EXAMPLE 13

Production of recombinant OCIF by 293/EBNA cells

i) Construction of the plasmid for expressing OCIF cDNA

pBKOCIF containing about 1.6 kb OCIF cDNA was prepared as described in EXAMPLE 11, and digested with restriction enzymes, BamHI and XhoI. The OCIF cDNA insert was cut out, separated by an agarose gel electrophoresis, and purified using QIAEX gel extraction kit (QIAGEN). The purified OCIF cDNA insert was ligated using DNA ligation kit ver. 2 (Takara Shuzo) to the expression vector pCEP4 (Invitrogen) digested with restriction enzymes, BamHI and XhoI. E.coli. DH5α (Gibco BRL) was transformed with the ligation mixture.

The transformants were grown and the plasmid containing the OCIF cDNA (about 1.6 kb) was purified using QIAGEN column (QIAGEN). The expression plasmid pCEPOCIF was precipitated with ethanol, and dissolved in sterile distilled water was used in the expreriments described below.

ii) Transient expression of OCIF cDNA and analysis of the biological activity

Recombinant OCIF was produced using the expression plasmid, pCEPOCIF prepared in EXAMPLE 13-i) according to the method described below. $8x10^5$ cells of 293/EBNA (Invitrogen) were inoculated in each well of the 6-well plate using IMDM containing 10 % fetal calf serum (Gibco BRL). After the cells were incubated for 24 hours, the culture medium was removed and the cells were washed with serum free IMDM. The expression plasmid, pCEPOCIF and lipofectamine (Gibco BRL) were diluted with OPTI-MEM (Gibco BRL) and were mixed, and added to the cells in each well according to the manufacture's instructions. Three μg of pCEPOCIF and 12 μl of lipofectamine were used for each transfection. After the cells were incubated with pCEPOCIF and lipofectamine for 38 hours, the medium was replaced with 1 ml of OPTI-MEM. After the transfected cells were incubated for 30 hours, the conditioned medium was harvested and used for the biological assay. The biological activity of OCIF was analysed according to the method described below. Bone marrow cells obtained from mice, 17 days-old, were suspended in α-MEM (manufactured by GIBCO BRL Co.) containing 10% FBS, $2x10^{-8}$M activated vitamin D_3 and each test sample, and were inoculatd and cultured for 7 days at 37℃ in humidified 5%CO_2 as described in EXAMPLE 2. During incubation, 160

μl of old medium in each well was replaced with the same volume of the fresh medium containing test sample diluted with $1x10^{-8}$M of activated vitamin D_3 and α-MEM containing FBS on day 3 and day 5. On day 7, after washing the wells with phosphate buffered saline, cells were fixed with ethanol/acetone (1:1) for 1 min. and then osteoclast development was tested using acid phosphatase activity mesuring kit (Acid Phosphatase, Leucocyte, Catalog No. 387-A, Sigma Co.). The decrease of the number of TRAP positive cells was taken as an OCIF activity. As result, the conditioned medium showed the same OCIF activity as natural OCIF protein from IMR-90 conditioned medium (Table 4).

Table 4

OCIF activity of 293/EBNA conditioned medium.

Cultured Cell	Dilution						
	1/20	1/40	1/80	1/160	1/320	1/640	1/1280
OCIF expression vector transfected	++	++	++	++	++	+	-
vector transfected	-	-	-	-	-	-	-
untreated	-	-	-	-	-	-	-

[++ ; OCIF activity inhibiting osteoclast development more than 80%, + ; OCIF activity inhibiting osteoclast development between 30% and 80%, and - ; no

OCIF activity.]

iii) Isolation of recombinant OCIF protein from 293/EBNA-conditioned medium

293/EBNA-conditioned medium (1.8 l) obtained by cultivating the cells described in example 13-ii) was supplemented with 0.1 % of CHAPS and filtrated with 0.22 μm membrane filter (Steribecs GS, Milipore Co.). The conditioned medium was applied to 50 ml of a heparin Sepharose CL-6B column (2.6 x 10 cm, Pharmacia Co.) equilibrated with 10mM Tris-HCl, pH 7.5. After washing the column with 10mM Tris-HCl, pH 7.5, the adsorbed protein was eluted from the column with linear gradient from 0 to 2 M NaCl at a flow rate of 4 ml/min for 100 min. and fractions (8 ml) were collected. Using 150 μl of each fraction, OCIF activity was assayed according to the method described in EXAMPLE 2. OCIF active fraction (112 ml) eluted with approximately 0.6 to 1.2 M NaCl was obtained.

One hundred twelve ml of the active fraction was diluted to 1000 ml with 10 mM Tris-HCl, 0.1% CHAPS, pH 7.5, and applied to a heparin affinity column (heparin-5PW, 0.8 x 7.5 cm, Tosoh Co.) equilibrated with 10mM Tris-HCl, 0.1% CHAPS, pH 7.5. After washing the column with 10mM Tris-HCl, 0.1% CHAPS, pH 7.5, the adsorbed protein was eluted from the column with linear gradient from 0 to 2 M NaCl at a flow rate of 0.5ml/min for 60 min., and fractions (0.5 ml) were collected. Four μl of each fraction was analyzed by SDS-polyacrylamide gel electrophoresis under reducing and non-reducing conditions as described in EXAMPLE 4. On SDS-PAGE under reducing conditions, a single band of rOCIF protein with an apparent 60 KD was detected in fractions from 30 to 32, under

non-reducing conditions, bands of rOCIF protein with an apparent 60 KD and 120 KD were also detected in fractions from 30 to 32. The isolated rOCIF fraction from 30 to 32 was designated as recombinant OCIF derived from 293/EBNA (rOCIF(E)). 1.5 ml of the rOCIF(E) (535 μg/ml) was obtained when determined by the method of Lowry using bovine serum albumin as a standard protein.

EXAMPLE 14

Production of recombinant OCIF using CHO cells

i) Construction of the plasmid for expressing OCIF

pBKOCIF containing about 1.6 kb OCIF cDNA was prepared as described in EXAMPLE 11, and digested with restriction enzymes, SalI and EcoRV. About 1.4 kb OCIF cDNA insert was separated by an agarose gel electrophoresis, and purified from the gel using QIAEX gel extraction kit (QIAGEN). The expression vector, pcDL-SR α296 (Molecular and Cellular Biology, vol 8, p466, 1988) was digested with restriction enzymes, PstI and KpnI. About 3.4 kb of the expression vector fragment was cut out, separated by agarose gel electrophoresis, and purified from the gel using QIAEX gel extraction kit (QIAGEN). The ends of the purified OCIF cDNA insert and the expression vector fragment were blunted using DNA blunting kit (Takara Shuzo). The purified OCIF cDNA insert and the expression vector fragment were ligated using DNA ligation kit ver. 2 (Takara Shuzo). E.coli. DH5a α (Gibco BRL) was transformed with the ligation mixture. The transformant containing the OCIF expression plasmid, pSRαOCIF was obtained.

ii) Preparation of expression plasmid

The transformant containing the OCIF expression plasmid, pSR αOCIF preprared in the example 13-i) and the transformant containing the mouse DHFR expression plasmid, pBAdDSV shown in WO92/01053 were grown according to the standard method. Both plasmids were purified by alkali treatment, polyethylene glycol precipitation, and cesium chrolide density gradient ultra centrifugation according to method of Maniatis et al. (Molecular cloning, 2nd edition).

iii) Adaptation of CHOdhFr- cells to the protein free medium

CHOdhFr- cells (ATCC, CRL 9096) were cultured in IMDM containing 10 % fetal calf serum. The cells were adapted to EX-CELL 301 (JRH Biosciecnce) and then adapted to EX-CELL PF CHO (JRH Biosciecnce) according to the manufacture's instructions.

iv) Transfection of the OCIF expression plasmid, and the mouse DHFR expression plasmid, to CHOdhFr- cells.

CHOdhFr- cells prepared in EXAMPLE 14-iii) were transfected by electroporation with pSRαOCIF and pBAdDSV prepared in EXAMPLE 14-ii). 200 μg of pSRαOCIF and 20 μg of pBAdDSV were dissolved under sterile conditions in 0.8 ml of IMDM (Gibco BRL) containing 10 % fetal calf serum CG. $2x10^7$ cells of CHOdhFr- were suspended in 0.8 ml of this medium. The cell suspension was transfered to a cuvette (Bio Rad) and the cells were transfected by electroporation using gene pulser (Bio Rad) under condition of

360 V and 960 μF. The suspension of electroporated cells was transferred to T-flasks (Sumitomo Bakelite) containing 10 ml of EX-CELL PF-CHO, and incubated in the CO_2 incubator for 2 days. Then the transfected cells were inoculated in each well of a 96 well plate (Sumitomo Bakelite) at a density of 5000 cells/well and cultured for about 2 weeks. The transformants expressing DHFR are selected since EX-CELL PF-CHO does not contain nucleotides and the parental cell line CHO dhFr- can not grow in this medium. Most of the transformants expressing DHFR express OCIF since the OCIF expression plasmid was used ten times as much as the mouse DHFR expression plasmid. The transformants whose conditioned medium had high OCIF activity were selected among the transformants expressing DHFR according to the method described in EXAMPLE 2. The transformants that express large amounts of OCIF were cloned by limiting dilution. The clones whose conditioned medium had high OCIF activity were selected as described above and the transformant expressing large amount of OCIF, 5561, was obtained.

v) Production of recombinant OCIF

To produce recombinant OCIF (rOCIF), EX-CELL 301 medium (3 l) in a 3 l-spiner flask was inoculated with the clone (5561) at a cell-density of $1x10^5$ cells/ml. The 5561 cells were cultured in a spiner flask at 37℃ for 4 to 5 days. When the concentration of the 5561 cells reached to $1x10^6$ cells/ml, about 2.7 l of the conditioned medium was harvested. Then about 2.7 l of EX-CELL 301 was added to the spiner flask and the 5561 cells were cultured repeatedly. About 20 l of the conditioned medium was harvested using the three spiner

flasks.

vi) Isolation of recombinant OCIF protein from CHO cells-conditioned medium

CHOcells-conditioned medium (1.0 l) described in EXAMPL 14-v) was supplemented with 1.0 g of CHAPS and filtrated with 0.22 μm membrane filter (Steribecks GS, Milipore Co.). The conditioned medium was applied to a heparin Sepharose-FF column (2.6 x 10 cm, Pharmacia Co.) equilibrated with 10 mM Tris-HCl, pH 7.5. After washing the column with 10 mM Tris-HCl, 0.1 % CHAPS, pH 7.5, the adsorbed protein was eluted from the column with linear gradient from 0 to 2 M NaCl at a flow rate of 4 ml/min for 100 min. and fractions (8 ml) were collected. Using 150μl of each fraction, OCIF activity was assayed according to the method described in EXAMPLE 2. Active fraction (112 ml) eluted with approximately 0.6 to 1.2 M NaCl was obtained.

The 112 ml of active fraction was diluted to 1200 ml with 10 mM Tris-HCl, 0.1% CHAPS, pH 7.5, and applied to a affinity column (blue-5PW, 0.5 x 5.0 cm, Tosoh Co.) equilibrated with 10 mM Tris-HCl, 0.1% CHAPS, pH 7.5. After washing the column with 10 mM Tris-HCl, 0.1% CHAPS, pH 7.5, the adsorbed protein was eluted from the column with linear gradient from 0 to 3 M NaCl at a flow rate of 0.5ml/min for 60 min., and fractions (0.5 ml) were collected. Four μl of each fraction was subjected to SDS-polyacrylamide gel electrophoresis under reducing and non-reducing conditions as described in EXAMPLE 4. On SDS-PAGE under reducing conditions, a single band of rOCIF protein with apparent 60 KD was detected in fractions 30 to 38, under non-reducing conditions, bands of rOCIF protein with apparent 60 KD and 120 KD were also detected in fractions

30 to 38. The isolated rOCIF fraction, 30 to 38, was designated as purified recombinant OCIF derived from CHO cells (rOCIF(C)). 4.5 ml of the rOCIF(C) (113 μg/ml) was obtained when determined by the method of Lowry using bovine serum albumin as a standard protein.

EXAMPLE 15

Determination of N-terminal amino acid sequence of rOCIFs

Each 3 μg of the isolated rOCIF(E) and rOCIF(C) was adsorbed to polyvinylidene difluoride (PVDF) membranes with Prospin (PERKIN ELMER Co.). The membranes were washed with 20 % ethanol and the N-terminal amino acid sequences of the adsorbed proteins were analyzed by protein sequencer (PROCISE 492, PERKIN ELMER Co.). The determined N-terminal amino acid sequence is shown in sequence No. 7.

The N-terminal amino acid of rOCIF(E) and rOCIF(C) was the 22th amino acid of glutamine from Met as translation starting point, as shown in sequence number 5. The 21 amino acids from Met to Gln were identified as a signal peptide. The N-terminal amino acid sequence of OCIF isolated from IMR-90 conditioned medium was undetectable. Accordingly, the N-terminal glutamine of OCIF may be blocked by converting from glutamine to pyroglutamine within culturing or purifing.

EXAMPLE 16

Biological activity of recombinant(r) OCIF and natural(n) OCIF

i) Inhibition of vitamin D_3 induced osteoclast formation from murine bone marrow cells

Each the rOCIF(E) and nOCIF sample was diluted with α-MEM (GIBCO BRL Co.) containing 10% FBS and 2×10^{-8}M of activated vitamin D_3 (a final concentration of 250 ng/ml). Each sample was serially diluted with the same medium, and 100 μl of each diluted sample was added to each well in 96-well

plates. Bone marrow cells obtained from mice, 17 days-old, were inoculated at a cell density of $3x10^5$ cells/100μl/ well to each well in 96-well plates and cultured for 7 days at 37℃ in humidified 5%CO_2. On day 7, the cells were fixed and stained with a acid phosphatase mesuring kit (Acid Phosphatase, Leucocyte, No387-A, Sigma) according to the method described in EXAMPLE 2. The decrease of acid phosphatase activity (TRAP) was taken as OCIF activity. The decrease of acid phosphatase-positive cells was evaluated by solubilizing the pigment of dye and measuring absorbance. In detail, 100 μl of a mixture of 0.1 N NaOH and dimethylsulfoxide (1:1) was added to each well and the well was vibrated to solubilize the dye. After solubilizing the dye completely, an absorbance of each well was measured at 590 nm subtracting the absorbance at 490 nm using microplate reader (Immunoreader NJ-2000, InterMed). The microplate reader was adjusted to 0 absorbance using a well with monolayered bone marrow cells which was cultured in the medium without activated vitamin D_3. The decrease of TRAP activity was expressed as a percentage of the control absorbance value (=100%) of the solubilized dye from wells with bone marrow cells which were cultured in the absence of OCIF. The results are shown in Table 5.

Table 5

Inhibition of vitamin D3-induced osteoclast formation from murine bone marrow cells

OCIF concentration(ng/ml)	250	125	63	31	16	0
rOCIF(E)	0	0	3	62	80	100

nOCIF	0	0	27	27	75	100 (%)

Both nOCIF and rOCIF(E) inhibited osteoclast formation in a dose dependent manner in the concentration of 16 ng/ml or higher

ii) Inhibition of vitamin D3-induced osteoclast formation in co-cultures of stromal cells and mouse spleen cells.

Effect of OCIF on osteoclast formation induced by Vitamin D_3 in co-cultures of stromal cells and mouse spleen cells was tested according to the method of N. Udagawa et al. (Endocrinology, vol. 125, p1805-1813, 1989). In detail, each of rOCIF(E), rOCIF(C), and nOCIF sample was serially diluted with α-MEM (GIBCO BRL Co.) containing 10% FBS, $2x10^{-8}$M of activated vitamin D_3, and $2x10^{-7}$M dexamethasone, and 100μl of each the diluted samples was added to each well in 96 well-microwell plates. Murine bone marrow-derived stromal ST2 cells (RIKEN Cell Bank RCB0224) ; $5x10^3$ cells per 100μl of α-MEM containing 10% FBS, and spleen cells from ddy mice, 8 weeks-old, ; $1x10^5$ cells per 100 μl in the same medium, were inoculated to each well in 96-well plates and cultured for 5 days at 37℃ in humidified 5%CO_2. On day 5, the cells were fixed and stained with a kit for acid phosphatase (Acid Phosphatase, Leucocyte, No387-A, Sigma). The decrease of acid phosphatase-positive cells was taken as OCIF activity. The decrease of acid phosphatase-positive cells was evaluated according to the method described in EXAMPLE 16-i). The results are shown in Table 6 ; rOCIF(E) and rOCIF(C), and Table 7 ; rOCIF(E) and nOCIF.

Table 6

Inhibition of osteoclast formation in co-cultures of stromal cells and mouse spleen cells.

OCIF concentration(ng/ml)	50	25	13	6	0	
rOCIF(E)	3	22	83	80	100	
rOCIF(C)	13	19	70	96	100	(%)

Table 7

Inhibition of osteoclast formation in co-cultures of stromal cells and mouse spleen cells.

OCIF concentration(ng/ml)	250	63	16	0	
rOCIF(E)	7	27	37	100	
rOCIF(C)	13	23	40	100	(%)

nOCIF, rOCIF(E) and rOCIF(C) inhibited osteoclast formation in a dose dependent manner in the concentration of 6 - 16 ng/ml or higher

iii) Inhibition of PTH-induced osteoclast formation from murine bone marrow cells.

Effect of OCIF on osteoclast formation induced by PTH was tested according to the method of N. Takahashi et al. (Endocrinology, vol. 122,

p1373-1382, 1988). In detail, each the rOCIF(E) and nOCIF sample (125 ng/ml) was serially diluted with α-MEM (manufactured by GIBCO BRL Co.) containing 10% FBS and $2x10^{-8}$M PTH, and 100μl of each the diluted samples was added to 96 well-plates. Bone marrow cells from ddy mice, 17 days-old, at a cell density of $3x10^5$ cells per 100μl of α-MEM containing 10% FBS were inoculated to each well in 96-wells plates and cultured for 5 days at 37℃ in humidified 5%CO_2. On day 5, the cells were fixed with ethanol/aceton (1:1) for 1 min. at room temperature and stained with a kit for acid phosphatase (Acid Phosphatase, Leucocyte, No387-A, Sigma) according to the method described in EXAMPLE 2. The decrease of acid phosphatase-positive cells was taken as OCIF activity. The decrease of acid phosphatase-positive cells was evaluated according to the method described in EXAMPLE 16-i). The results are shown in Table 8.

Table 8

Inhibition of PTH-induced osteoclast formation from murine bone marrow cells.

OCIF concentration(ng/ml)	125	63	31	16	8	0
rOCIF(E)	6	58	58	53	88	100
nOCIF	18	47	53	56	91	100

nOCIF and rOCIF(E) inhibited osteoclast formation in a dose dependent manner in the concentration of 16 ng/ml or higher

iv) Inhibition of IL-11-induced osteoclast formation

Effect of OCIF on osteoclast formation induced by IL-11 was tested according to the method of T. Tamura et al. (Proc. Natl. Acad. Sci. USA, vol. 90, p11924-11928, 1993). In detail, each rOCIF(E) and nOCIF sample was serially diluted with α-MEM (GIBCO BRL Co.) containing 10% FBS and 20 ng/ml IL-11 and 100μl of each the diluted sample was added to each well in 96-well plates. Newborn mouse calvaria-derived pre-adipocyte MC3T3-G2/PA6 cells (RIKEN Cell Bank RCB1127) ; $5x10^3$ cells per 100μl of α-MEM containing 10% FBS, and spleen cells from ddy mouse, 8 weeks-old, ; $1x10^5$ cells per 100 μl in the same medium, were inoculated to each well in 96-well plates and cultured for 5 days at 37 ℃ in humidified 5%CO_2. On day 5, the cells were fixed and stained with a kit for acid phosphatase (Acid Phosphatase, Leucocyte, No387-A, Sigma). Acid phosphatase positive cells were counted under microscope and a decrease of the cell numbers was taken as OCIF activity. The results are shown in Table 9.

Table 9

OCIF concentration(ng/ml)	500	125	31	7.8	2.0	0.5	0
nOCIF	0	0	1	4	13	49	31
rOCIF(E)	0	0	1	3	10	37	31

Both nOCIF and rOCIF(E) inhibited osteoclast formation in a dose dependent manner in the concentration of 2 ng/ml or higher

The results shown in Table 4-8 indicated that OCIF inhibits all the

vitamin D_3, PTH, and IL-11-induced osteoclast formations at almost the same doses. Accordingly, OCIF would be able to be used for treatment of the different types of bone disorders with decreased bone mass, which are caused by different substances which induce bone resorption.

EXAMPLE 17

Isolation of monomer-type OCIF and dimer-type OCIF

Each rOCIF(E) and rOCIF(C) sample containing 100 μg of OCIF protein, was supplemented with 1/100 volume of 25 % trifluoro acetic acid and applied to a reverse phase column (PROTEIN-RP, 2.0x250 mm, YMC Co.) equilibrated with 30 % acetonitrile containing 0.1 % trifluoro acetic acid. OCIF protein was eluted from the column with linear gradient from 30 to 55 % acetonitrile at a flow rate of 0.2 ml/min for 50 min. and each OCIF peak was collected. Each the monomer-type OCIF peak fraction and dimer-type OCIF peak fraction was lyophilized, respectively.

EXAMPLE 18

Determination of molecular weight of recombinant OCIFs

Each 1 μg of the isolated monomer-type and dimer-type nOCIF purified using reverse phase column according to EXAMPLE 3-iv) and each 1 μg of monomer-type and dimer-type rOCIF described in EXAMPLE 17 was concentrated under vaccum, respectively. Each sample was incubated in the buffer for SDS-PAGE, subjected to SDS-polyacrylamide gel electrophoresis, and protein bands on the gel were stained with silver according to the method described in

EXAMPLE 4. Results of electrophoresis under non-reducing conditions and reducing conditions are shown in Figure 6 and Figure 7.

A protein band with an apparent molecular weight of 60 KD was detected in each monomer-type OCIF sample, and a protein band with an apparent molecular weight of 120 KD was detected in each dimer-type OCIF sample in non-reducing conditions. A protein band with an apparent molecular weight of 60 KD was detected in each monomer-type OCIF sample under reducing conditions. Accordingly, molecular weights of monomer-type nOCIF from IMR-90 cells, rOCIF from 293/EBNA cells and rOCIF from CHO cells were almost the same. Molecular weights of dimer-type nOCIF from IMR-90 cells, rOCIF from 293/EBNA cells, and rOCIF from CHO cells were also the same.

EXAMPLE 19

Remove N-linked Oligosaccharide chain and Mesuring molecular weight of natural and recombinant OCIF

Each sample containing 5 μg of the isolated monomer-type and dimer-type nOCIF purified using reverse phase column according to EXAMPLE 3-iv) and each sample containing 5 μg of monomer-type and dimer-type rOCIF described in EXAMPLE 17 were concentrated under vaccum. Each sample was dissolved in 9.5 μl of 50 mM sodium phosphate buffer, pH 8.6, containing 100 mM 2-mercaptoethanol, supplemented with 0.5 μl of 250 U/ml N-glycanase (Seikagaku kogyo Co.) and incubated for one day at 37 ℃. Each sample was supplemented with 10 μl of 20 mM Tris-HCl, pH 8.0 containing 2 mM EDTA, 5 % SDS, and 0.02 % bromo-phenol blue and heated for 5 min at 100 ℃. Each 1 μl

of the samples was subjected to SDS-polyacrylamide gel electrophoresis, and protein bands on the gel were stained with silver as described in EXAMPLE 4. The patterns of electrophoresis are shown in Figure 8.

An apparent molecular weight of each the deglycosylated nOCIF from IMR-90 cells, rOCIF from CHO cells, and rOCIF from 293/EBNA cells was 40 KD under reducing conditions. An apparent molecular weight of each untreated nOCIF from IMR-90 cells, rOCIF from 293/EBNA cells, and rOCIF from CHO cells was 60 KD under reducing conditions. Accordingly, the results indicate that the OCIF proteins are glycoproteins with N-linked sugar chains.

EXAMPLE 20

Cloning of OCIF variant cDNAs and determination of their DNA squences

The plasmid pBKOCIF, which is inserted OCIF cDNA to pBKCMV (Stratagene), was obtained from one of some purified positive phage as in example 10 and 11. And more, during the screening of the cDNA library with the 397 bp OCIF cDNA probe, the transformants containing plasmids whose insert sizes were different from that of pBKOCIF were obtained. These transformants containing the plasmids were grown and the plasmids were purified according to the standard method. The sequence of the insert DNA in each plasmid was determined using Taq Dye Deoxy Terminater Cycle Sequencing kit (Perkin Elmer). The used primers were T3, T7 primers (Stratagene) and synthetic primers prepared based on the nucleotide sequence of OCIF cDNA. There are four OCIF variants (OCIF2, 3, 4, and 5) in addition to OCIF. The nucleotide sequence of OCIF2 is shown in the sequence number 8 and the amino acid sequence of OCIF 2 predicted by the nucleotide sequence is shown in the sequence number 9. The nucleotide sequence of OCIF3 is shown in the sequence number 10 and the amino acid sequence of OCIF3 predicted by the nucleotide sequence is shown in the sequence number 11. The nucleotide sequence of OCIF4 is shown in the sequence number 12 and the amino acid sequence of OCIF4 predicted by the nucleotide sequence is shown in the sequence number 13. The nucleotide sequence of OCIF5 is shown in the sequence number 14 and the amino acid sequence of OCIF5 predicted by the nucleotide sequence is shown in the sequence number 15. The structures of OCIF variants are shown in Figures 9 to 12 and are described in brief below.

OCIF2

OCIF2 cDNA has a deletion of 21 bp from guanine at nucleotide number 265 to guanine at nucleotide number 285 in OCIF cDNA (sequence number 6). Accordingly OCIF2 has a deletion of 7 amino acids from glutamic acid (Glu) at amino acid number 68 to glutamine (Gln) at amino acid number 74 in OCIF (sequence number 5).

OCIF3

OCIF3 cDNA has a point mutation at nucleotide number 9 in OCIF cDNA (sequence number 6) where cytidine is replaced with guanine. Accordingly OCIF3 has a mutation and asparagine (Asn) at amino acid number -19 in OCIF (sequence number 5) is replaced with lysine (Lys). The mutation seems to be located in the signal sequence and have no essential effect on the secreted OCIF3. OCIF3 cDNA has a deletion of 117 bp from guanine at nucleotide number 872 to cytidine at nucleotide number 988 in OCIF cDNA (sequence number 6).

Accordingly OCIF3 has a deletion of 39 amino acids from threonine (Thr) at amino acid number 270 to leucine (Leu) at amino acid number 308 in OCIF (sequence number 5).

OCIF4

OCIF4 cDNA has two point mutations in OCIF cDNA (sequence number 6). Cytidine at nucleotide number 9 is replaced with guanine and guanine at nucleotide number 22 is replaced with thymidine in OCIF cDNA (sequence number 6).

Accordingly OCIF4 has two mutations. Asparagine (Asn) at amino acid number -19 in OCIF (sequence number 5) is replaced with lysine (Lys), and alanine (Ala)

at amino acid number -14 is replaced with serine (Ser). These mutations seem to be located in the signal sequence and have no essential effect on the secreted OCIF4.

OCIF4 cDNA has about 4 kb DNA, which is the intron 2 of OCIF gene, inserted between nucleotide number 400 and nucleotide number 401 in OCIF cDNA (sequence number 6). The open reading frame stops in intron 2.

Accordingly OCIF4 has an additional novel amino acid sequence containing 21 amino acids after alanine (Ala) at amino acid number 112 in OCIF (sequence number 5).

OCIF5

OCIF5 cDNA has a point mutation at nucleotide number 9 in OCIF cDNA (sequence number 6) where cytidine is replaced with guanine.

Accordingly OCIF5 has a mutation and asparagine (Asn) at amino acid number -19 in OCIF (sequence number 5) is replaced with lysine (Lys). The mutation seems to be located in the signal sequence and have no essential effect on the secreted OCIF5.

OCIF5 cDNA has the latter portion (about 1.8 kb) of intron 2 between nucleotide number 400 and nucleotide number 401 in OCIF cDNA (sequence number 6). The open reading frame stops in the latter portion of intron 2.

Accordingly OCIF5 has an additional novel amino acid sequence containing 12 amino acids after alanine (Ala) at amino acid number 112 in OCIF (sequence number 5).

EXAMPLE 21

Production of OCIF variants

i) Construction of the plasmid for expressing OCIF variants

The plasmid containing OCIF2 or OCIF3 cDNA was obtained as described in EXAMPLE 20 and called pBKOCIF2 and pBKOCIF3, respectively. pBKOCIF2 and pBKOCIF3 were digested with restriction enzymes, BamHI and XhoI. The OCIF2 and OCIF3 cDNA inserts were separated by agarose gel electrophoresis, and purified from the gel using QIAEX gel extraction kit (QIAGEN). The purified OCIF2 and OCIF3 cDNA inserts were individually ligated using DNA ligation kit ver. 2 (Takara Shuzo) to the expression vector pCEP4 (Invitrogen) that had been digested with restriction enzymes, BamHI and XhoI. E.coli. DH5α (Gibco BRL) was transformed with the ligation mixture.

The plasmid containing OCIF4 cDNA was obtained as described in EXAMPLE 20 and called pBKOCIF4. pBKOCIF4 was digested with restriction enzymes, SpeI and XhoI (Takara Shuzo). The OCIF4 cDNA insert was separated by an agarose gel electrophoresis, and purified from the gel using QIAEX gel extraction kit (QIAGEN). The purified OCIF4 cDNA insert was ligated using DNA ligation kit ver. 2 (Takara Shuzo) to the expression vector pCEP4 (Invitrogen) that had been digested with restriction enzymes, NheI and XhoI (Takara Shuzo). E.coli. DH5 α (Gibco BRL) was transformed with the ligation mixture.

The plasmid containing OCIF5 cDNA was obtained as described in EXAMPLE 20 and was called pBKOCIF5. pBKOCIF5 was digested with restriction enzyme, HindIII (Takara Shuzo). The 5'portion of the coding region in the OCIF5 cDNA insert was separated by agarose gel electrophoresis, and purified from the gel using QIAEX gel extraction kit (QIAGEN). The OCIF expression plasmid, pCEPOCIF,

obtained in EXAMPLE 13-i) was digested with restriction enzyme, HindIII (Takara Shuzo). The 5'portion of the coding region in the OCIF cDNA was removed. The rest of the plasmid that contains pCEP vector and the 3'portion of the coding region of OCIF cDNA was called pCEPOCIF-3'. pCEPOCIF-3' was separated by an agarose gel electrophoresis, and purified from the gel using QIAEX gel extraction kit (QIAGEN). The OCIF5 cDNA HindIII fragment and pCEPOCIF-3' were ligated using DNA ligation kit ver. 2 (Takara Shuzo). E.coli. DH5 α (Gibco BRL) was transformed with the ligation mixture.

The obtained transformants were grown at 37 ℃ overnight and the OCIF variants expression plasmids (pCEPOCIF2, pCEPOCIF3, pCEPOCIF4, and pCEPOCIF5) were purified using QIAGEN column (QIAGEN). These OCIF-variants-expression plasmids were precipitated with ethanol, dissolved in sterile distilled water, and used in the exprerіments described below.

ii) Transient expression of OCIF variant cDNAs and analysis of the biological activity of recombinant OCIF variants.

Recombinant OCIF variants were produced using the expression plasmid, pCEPOCIF2, pCEPOCIF3, pCEPOCIF4, and pCEPOCIF5 prepared as described in EXAMPLE 21-i) according to the method described in EXAMPLE 13-ii). The biological activities of recombinant OCIF variants were analysed. The results were that these OCIF variants (OCIF2, OCIF3, OCIF4, and OCIF5) had a weak activity.

EXAMPLE 22

Preparation of OCIF mutants

i) Construction of a plasmid vector for subcloning cDNAs encoding OCIF mutants

The plasmid vector (5 μg) described in EXAMPLE 11 was digested with restriction enzymes Bam HI and Xho I (Takara Shuzo). The digested DNA was subjected to a preparative agarose gel electrophoresis. DNA fragment with an approximate size of 1.6 kilobase pairs (kb) that contained the entire coding sequence for OCIF was purified from the gel using QIAEX gel extraction kit (QIAGEN). The purified DNA was dissolved in 20 μl of sterile distilled water. This solution was designated DNA solution 1. p Bluescript II SK + (3 μg) (Stratagene) was digested with restriction enzymes Bam HI and Xho I (Takara Shuzo). The digested DNA was subjected to preparative agarose gel electrophoresis. DNA fragment with an approximate size of 3.0 kb was purified from the gel using QIAEX DNA extraction kit (QIAGEN). The purified DNA was dissolved in 20 μl of sterile distilled water. The solution was designated DNA solution 2. One microliter of DNA solution 2, 4 μl of DNA solution 1 and 5 μl of ligation buffer I of DNA ligation kit ver. 2 (Takara Shuzo) were mixed and incubated at 16 ℃ for 30 min. (The ligation mixture was used for the transformation of E. coli in a manner described below). Conditions for transformation of E. coli were as follows. One hundred microliters of competent E. coli DH5 α cells (GIBCO BRL) and 5μl of the ligation mixture was mixed in a sterile 15-ml tube (IWAKI glass). The tube was kept on ice for 30 min. After incubation for 45 sec at 42℃, to the cells was added 250 μl of L broth (1% Tryptone, 0.5% yeast extract, 1% NaCl). The cell suspension was then incubated for 1hr. at 37℃ with shaking. Fifty

microliters of the cell suspension was plated onto an L-agar plate containing 50 μg/ml of ampicillin. The plate was incubated overnight at 37℃.

Six colonies which grew on the plate were individually incubated in 2 ml each of L-broth containing 50 μg/ml of ampicillin overnight at 37℃ with shaking. The structure of the plasmids in the colonies was analyzed. A plasmid in which the 1.6-kb DNA fragment containing the entire OCIF cDNA is inserted between the digestion sites of Bam HI and Xho I of pBluescript II SK + was obtained and designated as pSK + -OCIF.

ii) Preparation of mutants in which one of the Cys residues in OCIF is replaced with Ser residue

1) Introduction of mutations into OCIF cDNA

OCIF mutants were prepared in which one of the five Cys residues present in OCIF at positions 174, 181, 256, 298 and 379 (in SEQUENCE NO 4) was replaced with Ser residue and were designated OCIF-C19S(174Cys to Ser), OCIF-C20S (181Cys to Ser), OCIF-C21S (256Cys to Ser), OCIF-C22S (298Cys to Ser) and OCIF-C23S (379Cys to Ser), respectively.

To prepare the mutants, nucleotides encoding the corresponding Cys residues were replaced with those encoding Ser. Mutagenesis was carried out by a two-step polymerase chain reaction (PCR). The first step of the PCRs consisted of two reactions, PCR 1 and PCR 2.

PCR 1	10X Ex Taq Buffer (Takara Shuzo)	10 μl
	2.5 mM solution of dNTPs	8 μl
	the plasmid vector described in EXAMPLE 11 (8ng/ml)	2 μl
	sterile distilled water	73.5 μl

	20 μM solution of primer 1	5 μl
	100 μM solution of primer 2 (for mutagenesis)	1 μl
	Ex Taq (Takara Shuzo)	0.5 μl
PCR 2	10X Ex Taq Buffer (Takara Shuzo)	10 μl
	2.5 mM solution of dNTPs	8 μl
	the plasmid vector described in EXAMPLE 11 (8ng/ml)	2 μl
	sterile distilled water	73.5 μl
	20 μM solution of primer 3	5 μl
	100 μM solution of primer 4 (for mutagenesis)	1 μl
	Ex Taq (Takara Shuzo)	0.5 μl

Specific sets of primers were used for each mutation and other components were unchanged. Primers used for the reactions are shown in Table 10. The nucleotide sequences of the primers are shown in SEQUENCE NO: 20, 23, 27 and 30-40. The PCRs were performed under the following conditions as follows. An initial denaturation step at 97℃ for 3 min was followed by 25 cycles of denaturation at 95℃ for 1 min annealing at 55℃ for 1 min and extension at 72℃ for 3 min. After these amplification cycles, final extension was performed at 70℃ for 5 min. The size of the PCR prodcts was confirmed by agarose gel electrophoresis using reaction solution. After the first PCR, excess primers were removed using Amicon microcon (Amicon). The final volume of the solutions that contained the PCR products were made to 50μl with sterile distilled water. These purified PCR products were used for the second PCR (PCR 3).

PCR 3	10X Ex Taq Buffer (Takara Shuzo)	10 μl

2.5 mM solution of dNTPs	8 μl
solution containing DNA fragment obtained from PCR 1	5 μl
solution containing DNA fragment obtained from PCR 2	5 μl
sterile distilled water	61.5 μl
20 μM solution of primer 1	5 μl
20 μM solution of primer 3	5 μl
Ex Taq (Takara Shuzo)	0.5 μl

Table 10

mutants	primer-1	primer-2	primer-3	primer-4
OCIF-C19S	IF 10	C19SR	IF 3	C19SF
OCIF-C20S	IF 10	C20SR	IF 3	C20SF
OCIF-C21S	IF 10	C21SR	IF 3	C21SF
OCIF-C22S	IF 10	C22SR	IF 14	C22SF
OCIF-C23S	IF 6	C23SR	IF 14	C23SF

The reaction conditions were exactly the same as those for PCR 1 or PCR 2. The size of the PCR prodcts was confirmed by 1.0 % or 1.5 % agarose gel electrophoresis. The DNA fragments were precipitated with ethanol, dried under vacuum and dissolved in 40 μl of sterile distilled water. The solutions containing DNA fragments with mutation C19S, C20S, C21S, C22S and C23S were

designated as DNA solution A, DNA solution B, DNA solution C, DNA solution D and DNA solution E, respectively.

The DNA fragment which is contained in solution A (20 μl) was digested with restriction enzymes Nde I and Sph I (Takara Shuzo). A DNA fragment with an approximate size of 400 base pairs (bp) was extracted from a preparative agarose gel and dissolved in 20 μl of sterile distilled water. This DNA solution was designated DNA solution 3. Two micrograms of pSK + -OCIF was digested with restriction enzymes Nde I and Sph I. A DNA fragment with an approximate size of 4.2 kb was purified from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20 μl of sterile distilled water. This DNA solution was designated as DNA solution 4. Two microliters of DNA solution 3, 3 μl of DNA solution 4 and 5 μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation reaction was carried out. Competent E. coli DH5 α cells were transformed with 5 μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-C19S.

The DNA fragment which is contained in solution B (20 μl) was digested with restriction enzymes Nde I and Sph I. A DNA fragment with an approximate size of 400 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20μl of sterile distilled water. This DNA solution was designated DNA solution 5. Two microliters of DNA solution 5, 3 μl of DNA solution 4 and 5 μl of ligation buffer I of DNA ligation kit

ver. 2 were mixed and ligation reaction was carried out. Competent E. coli DH5 α cells were transformed with 5 μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-C20S.

The DNA fragment which is contained in solution C (20 μl) was digested with restriction enzymes Nde I and Sph I. A DNA fragment with an approximate size of 400 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20μl of sterile distilled water. This DNA solution was designated as DNA solution 6. Two microliters of DNA solution 6, 3 μl of DNA solution 4 and 5μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation reaction was carried out. Competent E. coli DH5 α cells were transformed with 5 μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-C21S.

The DNA fragment which is contained in solution D (20 μl) was digested with restriction enzymes Nde I and Bst PI. A DNA fragment with an approximate size of 600 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20 μl of sterile distilled water. This DNA solution was designated as DNA solution 7. Two micrograms of pSK + -OCIF was digested with restriction enzymes Nde I and Bst PI. A DNA fragment with an approximate size of 4.0 kb was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20μl of sterile distilled

water. This DNA solution was designated as DNA solution 8. Two microliters of DNA solution 7, 3 μl of DNA solution 8 and 5μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation reaction was carried out. Competent E. coli DH5 α cells were transformed with 5 μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA in which the 600-bp Nde I-BstPI fragment with the mutation (the C22S mutation) is substituted for the 600-bp Nde I-Bst PI fragment of pSK+ -OCIF by analyzing the DNA structure. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-C22S.

The DNA fragment which is contained in solution E (20 μl) was digested with restriction enzymes Bst PI and Eco RV. A DNA fragment with an approximate size of 120 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20μl of sterile distilled water. This DNA solution was designated as DNA solution 9. Two micrograms of pSK + -OCIF was digested with restriction enzymes Bst EII and Eco RV. A DNA fragment with an approximate size of 4.5 kb was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20μl of sterile distilled water. This DNA solution was designated as DNA solution 10. Two microliters of DNA solution 9, 3 μl of DNA solution 10 and 5 μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation was carried out. Competent E. coli DH5 α cells were transformed with 5μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by

DNA sequencing. The plasmid thus obtained was named pSK-OCIF-C23S.

2) Construction of vectors for expressing the OCIF mutants

pSK-OCIF-C19S, pSK-OCIF-C20S, pSK-OCIF-C21S, pSK-OCIF-C22S and pSK-OCIF-C23S were digested with restriction enzymes Bam HI and Xho I. The 1.6 kb Bam HI-Xho I DNA fragment encoding each OCIF mutant was isolated and dissolved in 20 μl of sterile distilled water. The DNA solutions that contain 1.6 kb cDNA fragments derived from pSK-OCIF-C19S, pSK-OCIF-C20S, pSK-OCIF-C21S, pSK-OCIF-C22S and pSK-OCIF-C23S were designated C19S DNA solution, C20S DNA solution, C21S DNA solution, C22S DNA solution and C23S DNA solution, respectively. Five micrograms of a expression vector pCEP 4 (Invitrogen) was digested with restriction enzymes Bam HI and Xho I. A DNA fragment with an approximate size of 10 kb was purified and dissolved in 40 μl of sterile distilled water. This DNA solution was designated as pCEP 4 DNA solution. One microliter of pCEP 4 DNA solution and 6 μl of either C19SDNA solution, C20S DNA solution, C21S DNA solution, C22S DNA solution or C23S DNA solution were independently mixed with 7 μl of ligation buffer I of DNA ligation kit ver. 2 and ligation reactions were carried out. Competent E. coli DH5α cells (100 μl) were transformed with 7 μl of each ligation mixture. Ampicillin-resistant transformants were screened for clones containing plasmid in which a 1.6-kb cDNA fragment is inserted between the recognition sites of Bam HI and Xho I of pCEP 4 by analyzing the DNA structure. The plasmide which were obtained containing the cDNA encoding OCIF-C19S, OCIF-C20S, OCIF-C21S, OCIF-C22S and OCIF-C23S were designated pCEP4-OCIF-C19S, pCEP4-OCIF-C20S, pCEP4-OCIF-C21S, pCEP4-OCIF-C22S and

pCEP4-OCIF-C23S, respectively.

ii) Preparation of domain-deletion mutants of OCIF

(1) deletion mutagenesis of OCIF cDNA

A series of OCIF mutants with deletions of from Thr 2 to Ala 42, from Pro 43 to Cys 84, from Glu 85 to Lys 122, from Arg 123 to Cys 164, from Asp 177 to Gln 251 and from Ile 252 to His 326 were prepared (positions of the amino acid residues are shown in SEQUENCE NO: 4). These mutants were designated as OCIF-DCR1, OCIF-DCR2, OCIF-DCR3, OCIF-DCR4, OCIF-DDD1 and OCIF-DDD2, respectively.

Mutagenesis was performed by two-step PCR as described in EXAMPLE 22-(ii). The primer sets for the reactions are shown in Table 11 and the nucleotide sequences of the primers are shown in SEQUENCE NO:19, 25, 40-53, and 54.

Table 11

mutants	primer-1	primer-2	primer-3	primer-4
OCIF-DCR1	XhoI F	DCR1R	IF 2	DCR1F
OCIF-DCR2	XhoI F	DCR2R	IF 2	DCR2F
OCIF-DCR3	XhoI F	DCR3R	IF 2	DCR3F
OCIF-DCR4	XhoI F	DCR4R	IF 16	DCR4F
OCIF-DDD1	IF 8	DDD1R	IF 14	DDD1F
OCIF-DDD2	IF 8	DDD2R	IF 14	DDD2F

The final PCR products were precipitated with ethanol, dried under vacuum and dissolved in 40 μl of sterile distilled water. Solutions of DNA fragment coding for portions of OCIF-DCR1, OCIF-DCR2, OCIF-DCR3, OCIF-DCR4, OCIF-DDD1 and OCIF-DDD2 were designated as DNA solutions F, G, H, I, J and K, respectively.

The DNA fragment which is contained in solution F (20 μl) was digested with restriction enzymes Nde I and Xho I. A DNA fragment with an approximate size of 500 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20 μl of sterile distilled water. This DNA solution was designated DNA solution 11. Two micrograms of pSK+ -OCIF was digested with restriction enzymes Nde I and Xho I. A DNA fragment with an approximate size of 4.0 kb was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20 μl of sterile distilled water. This DNA solution was designated DNA solution 12. Two microliters of DNA solution 11, 3 μl of DNA solution 12 and 5 μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation was carried out. Competent E. coli DH5 α cells were transformed with 5 μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-DCR1.

The DNA fragment which is contained in solution G (20 μl) was digested with restriction enzymes Nde I and Xho I. A DNA fragment with an approximate size of 500 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20 μl of sterile distilled water. This DNA

solution was designated as DNA solution 13. Two microliters of DNA solution 13, 3 μl of DNA solution 12 and 5 μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation was carried out. Competent E. coli DH5a cells were transformed with 5 μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing plasmid DNA . DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-DCR2.

The DNA fragment which is contained in solution H (20 μl) was digested with restriction enzymes Nde I and Xho I. A DNA fragment with an approximate size of 500 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20μl of sterile distilled water. This DNA solution was designated as DNA solution 14. Two microliters of DNA solution 14, 3 μl of DNA solution 12 and 5 μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation reaction was carried out. Competent E. coli DH5 α cells were transformed with 5 μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-DCR3.

The DNA fragment which is contained in solution I (20 μl) was digested with restriction enzymes Xho I and Sph I. A DNA fragment with an approximate size of 900 bp was extracted from a preparative agarose gel with QIAEX gel

extraction kit and dissolved in 20 μl of sterile distilled water. This DNA solution was designated as DNA solution 15. Two micrograms of pSK+ -OCIF was digested with restriction enzymes Xho I and Sph I. A DNA fragment with an approximate size of 3.6 kb was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20 μl of sterile distilled water. This DNA solution was designated as DNA solution 16. Two microliters of DNA solution 15, 3 μl of DNA solution 16 and 5 μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation reaction was carried out. Competent E. coli DH5 α cells were transformed with 5 μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-DCR4.

The DNA fragment which is contained in solution J (20 μl) was digested with restriction enzymes BstP I and Nde I. A DNA fragment with an approximate size of 400 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20 μl of sterile distilled water. This DNA solution was designated as DNA solution 17. Two microliters of DNA solution 17, 3 μl of DNA solution 8 and 5μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation reaction was carried out. Competent E. coli DH5 α cells were transformed with 5μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-DDD1.

The DNA fragment which is contained in solution K (20 μl) was digested with restriction enzymes Nde I and BstP I. A DNA fragment with an approximate size of 400 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20 μl of sterile distilled water. This DNA solution was designated as DNA solution 18. Two microliters of DNA solution 18, 3 μl of DNA solution 8 and 5μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation reaction was carried out. Competent E. coli DH5 α cells were transformed with 5 μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-DDD2.

2) Construction of vectors for expressing the OCIF mutants

pSK-OCIF-DCR1, pSK-OCIF-DCR2, pSK-OCIF-DCR3, pSK-OCIF-DCR4, pSK-OCIF-DDD1 and pSK-OCIF-DDD2 were digested with restriction enzymes Bam HI and Xho I. The Bam HI-Xho I DNA fragment containing entire coding sequence for each OCIF mutant was isolated and dissolved in 20 μl of sterile distilled water. These DNA solutions that contain the Bam HI-Xho I fragment derived from pSK-OCIF-DCR1, pSK-OCIF-DCR2, pSK-OCIF-DCR3, pSK-OCIF-DCR4, pSK-OCIF-DDD1 and pSK-OCIF-DDD2 were designated DCR1 DNA solution, DCR2 DNA solution, DCR3 DNA solution, DCR4 DNA solution, DDD1 DNA solution and DDD2 DNA solution, respectively. One microliter of pCEP 4 DNA solution and 6μl of either DCR1 DNA solution, DCR2 DNA solution, DCR3 DNA solution, DCR4 DNA solution, DDD1 DNA solution or DDD2 DNA solution were independently mixed with 7μl of

ligation buffer I of DNA ligation kit ver. 2 and ligation reactions were carried out. Competent E. coli DH5α cells (100 μl) were transformed with 7 μl of each ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA in which the DNA fragment with deletions is inserted between the recognition sites of Bam HI and Xho I of pCEP 4 by analyzing the DNA structure. The plasmids containing the cDNA encoding OCIF-DCR1, OCIF-DCR2, OCIF-DCR3, OCIF-DCR4, OCIF-DDD1 and OCIF-DDD2 were designated as pCEP4-OCIF-DCR1, pCEP4-OCIF-DCR2, pCEP4-OCIF-DCR3, pCEP4-OCIF-DCR4, pCEP4-OCIF-DDD1 and pCEP4-OCIF-DDD2, respectively.

iii) Preparation of OCIF with C-terminal domain truncation

(1) mutagenesis of OCIF cDNA

A series of OCIF mutants with deletions of from Cys at amino acid residue 379 to Leu 380, from Ser 331 to Leu 380, from Asp 252 to Leu 380, from Asp 177 to Leu 380, from Arg 123 to Leu 380 and from Cys 86 to Leu 380 was prepared. Positions of the amino acid residues are shown in SEQUENCE NO: 4. These mutants were designated as OCIF-CL, OCIF-CC, OCIF-CDD2, OCIF-CDD1, OCIF-CCR4 and OCIF-CCR3, respectively.

Mutagenesis for OCIF-CL was performed by the two-step PCR as described in EXAMPLE 22-(ii). The primer set for the reaction is shown in Table 12. The nucleotide sequences of the primers are shown in SEQUENCE NO:23, 40, 55, and 56. The final PCR products were precipitated with ethanol, dried under vacuum and dissolved in 40μl of sterile distilled water. This DNA solution was designated as solution L.

The DNA fragment which is contained in solution L (20 μl) was digested with restriction enzymes BstP I and EcoR V. A DNA fragment with an approximate size of 100 bp was extracted from a preparative agarose gel with QIAEX gel extraction kit and dissolved in 20μl of sterile distilled water. This DNA solution was designated as DNA solution 19. Two microliters of DNA solution 19, 3 μl of DNA solution 10 (described in EXAMPLE 22-(ii)) and 5μl of ligation buffer I of DNA ligation kit ver. 2 were mixed and ligation reaction was carried out. Competent E. coli DH5 α cells were transformed with 5μl of the ligation mixture. Ampicillin-resistant transformants were screened for a clone containing a plasmid DNA. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmid thus obtained was named pSK-OCIF-CL Mutagenesis of OCIF cDNA to prepare OCIF-CC, OCIF-CDD2, OCIF-CDD1, OCIF-CCR4 and OCIF-CCR3 was performed by a one-step PCR.

PCR reactions for mutagenesis to prepare OCIF-CC, OCIF-CDD2, OCIF-CDD1, OCIF-CCR4 and OCIF-CCR3

10X Ex Taq Buffer (Takara Shuzo)	10 μl
2.5 mM solution of dNTPs	8 μl
the plasmid vector containing the entire OCIF cDNA described in EXAMPLE 11 (8ng/ml)	2 μl
sterile distilled water	73.5 μl
20 μM solution of primer OCIF Xho F	5 μl
100 μM solution of primer (for mutagenesis)	1 μl
Ex Taq (Takara Shuzo)	0.5 μl

Table 12

mutants	primer-1	primer-2	primer-3	primer-4
OCIF-CL	IF 6	CL R	IF 14	CL F

Specific primers were used for each mutagenesis and other components were unchanged.

Primers used for the mutagenesis are shown in Table 13. Their nucleotide sequences are shown in SEQUENCE NO:57-61. The components of each PCR were mixed in a microcentrifuge tube and PCR was performed as follows. The microcentrifuge tubes were treated for 3 minutes at 97 ℃ and then incubated sequentially, for 30 seconds at 95 ℃, 30 seconds at 50 ℃ and 3 minutes at 70 ℃. This three-step incubation procedure was repeated 25 times, and after that, the tubes were incubated for 5 minutes at 70 ℃. An aliquot of the reaction mixture was removed from each tube and analyzed by an agarose gel electrophoresis to confirm the size of each product.

The size of the PCR products was confirmed on an agarose gel. Excess primers in the PCRs were removed using Amicon microcon (Amicon) after completion of the reaction. The DNA fragments were precipitated with ethanol, dried under vacuum and dissolved in 40 μl of sterile distilled water. The DNA fragment in each DNA solution was digested with restriction enzymes Xho I and Bam HI. After the reactions, DNA was precipitated with ethanol, dried under vacuum and dissolved in 20μl of sterile distilled water.

The solutions containing DNA fragment with the CC deletion, the CDD2

deletion, the CDD1 deletion, the CCR4 deletion and the CCR3 deletion were designated as CC DNA solution, CDD2 DNA solution, CDD1 DNA solution, CCR4 DNA solution and CC R3 DNA solution, respectively.

Table 13

mutants	primers for the mutagenesis
OCIF-CC	CC R
OCIF-CDD2	CDD2 R
OCIF-CDD1	CDD1 R
OCIF-CCR4	CCR4 R
OCIF-CCR3	CCR3 R

(2) Construction of vectors for expressing the OCIF mutants

pSK-OCIF-CL was digested with restriction enzymes Bam HI and Xho I. The Bam HI-Xho I DNA fragment containing the entire coding sequence for OCIF-CL was isolatedand dissolved in 20 μl of sterile distilled water. This DNA solution was designated as CL DNA solution. One microliter of pCEP 4 DNA solution and 6 μl of either of CL DNA solution, CC DNA solution, CDD2 DNA solution, CDD1 DNA solution, CCR4 DNA solution or CCR3 DNA solution were independently mixed with 7 μl of ligation buffer I of DNA ligation kit ver. 2 and ligation reactions were carried out. Competent E. coli DH5α cells (100 μl) were transformed with 7 μl of each ligation mixture. Ampicillin-resistant transformants were screened for clones containing plasmids which have the

desirable mutations in OCIF cDNA by analyzing the DNA structure. In each plasmid, OCIF cDNA fragment having a deletion were inserted between the recognition sites of Xho I and Bam HI of pCEP 4. The plasmids containing the cDNA encoding OCIF-CL, OCIF-CC, OCIF-CDD1, OCIF-CDD2, OCIF-CCR4 and OCIF-CCR3 were designated pCEP4-OCIF-CL, pCEP4-OCIF-CC, pCEP4-OCIF-CDD2, pCEP4-OCIF-CDD1, pCEP4-OCIF-CCR4 and pCEP4-OCIF-CCR3, respectively.

iv) Preparation of OCIF mutants with C-terminal truncation

(1) Introduction of C-terminal truncation to OCIF

A series of OCIF mutants with C-terminal truncation was prepared. OCIF mutant in which 10 residues of from Gln at 371 to Leu at 380 are replaced with 2 residues of Leu-Val was designated OCIF-CBst. OCIF mutant in which 83 residues of from Cys 298 to Leu 380 are replaced with 3 residues of Ser-Leu-Asp was designated OCIF-CSph. OCIF mutant in which 214 residues of from Asn 167 to Leu 380 are removed was designated OCIF-CBsp. OCIF muatant in which 319 residues of from Asp 62 to Leu 380 are replaced with 2 residues of Leu-Val was designated OCIF-CPst. Positions of the amino acid residues are shown in SEQUENCE NO: 4.

Two micrograms each of pSK + -OCIF was digested with one of the restriction enzymes, Bst PI, Sph I, PstI (Takara Shuzo), and Bsp EI (New England Biolabs), and followed by phenol extraction and ethanol precipitation. The precipitated DNA was dissolved in 10 μl of sterile distilled water. Ends of the DNAs in 2 μl of each solution were blunted using a DNA blunting kit in final volumes of 5 μl. To the reaction mixtures, 1 μg (1 μl) of an Amber

codon-containing Xba I linker (5'-CTAGTCTAGACTAG-3') and 6 μl of ligation buffer I of DNA ligation kit ver. 2 were added.

After the ligation reactions, 6 μl each of the reaction mixtures was used to transform E. coli DH5α. Ampicillin-resistant transformants were screened for clones containing plasmids. DNA structure was analyzed by restriction enzyme mapping and by DNA sequencing. The plasmids thus obtained were named pSK-OCIF-CBst, pSK-OCIF-CSph, pSK-OCIF-CBsp and pSK-OCIF-CPst, respectively.

(2) Construction of vectors for expressing the OCIF mutants

pSK-OCIF-CBst, pSK-OCIF- CSph, pSK-OCIF-CBsp and pSK-OCIF-CPst were digested with restriction enzymes Bam HI and Xho I. The 1.5 kb of DNA fragment containing entire coding sequence for each OCIF mutant was isolated and dissolved in 20 μl of sterile distilled water. These DNA solutions that contain the Bam HI-XhoI fragment derived from pSK-OCIF-CBst, pSK-OCIF- CSph, pSK-OCIF-CBsp and pSK-OCIF-CPst were designated as CBst DNA solution, CSph DNA solution, CBsp DNA solution and CPst DNA solution, respectively. One microliter of pCEP 4 DNA solution (described in EXAMPLE 22-ii)) and 6 μl of either CBst DNA solution, CSph DNA solution, CBsp DNA solution or CPst DNA solution were independently mixed with 7 μl of ligation buffer I of DNA ligation kit ver. 2 and ligation reactions were carried out. Competent E. coli DH5α cells (100 μl) were transformed with 7 μl of each ligation mixture. Ampicillin-resistant transformants were screened for clones containing plasmids in which cDNA fragment is inserted between the recognition sites of Bam HI and Xho I of pCEP 4 by analyzing the DNA structure. The plasmids containing the cDNA encoding OCIF-CBst, OCIF-CSph, OCIF-CBsp and OCIF-CPst

were designated as pCEP4-OCIF-CBst, pCEP4-OCIF- CSph, pCEP4-OCIF-CBsp and pCEP4-OCIF-CPst, respectively.

v) Preparetion of vectors for expressing the OCIF mutants

E. coli clones harboring the expression vectors for OCIF mutants (total of 21 clones) were grown and the vectors were purified by QIAGEN column (QIAGEN). All the expression vectors were precipitated with ethanol and dissolved in appropriate volumes of sterile distilled water and used for further manipupations shown below.

vi) Transient expression of the cDNAs for OCIF′ mutants and biological activities of the mutants

OCIF mutants were produced using the expression vectors prepared in EXAMPLE 22-v). The method was essentially the same as described in EXAMPLE 13. Only the modified points are described below. A 24-well plate was used for the DNA transfection. $2X10^5$ cells of 293/EBNA suspended in IMDM containing 10% fetal bovine serum were seeded into each well of the plate. One microgram of purified vector DNA and $4\mu l$ of lipofectamine were used for each transfection. Mixture of an expression vector and lipofectamine in OPTI-MEM (GIBCO BRL) in a final volume of 0.5 ml was added to the cells in a well. After the cells were incubated at 37℃ for 24 hr in a CO_2 incubator, the medium was replaced with 0.5 ml of Ex-cell 301 medium (JSR). The cells were incubated at 37 ℃ for 48 more hours in the CO_2 incubator. The conditioned medium was collected and used for assay for in vitro biological activity. The nucleotide sequences of cDNAs for the OCIF mutants are shown in SEQUENCE NO:83-103. The deduced amino acid sequences for the OCIF mutants are shown in SEQUENCE NO:

62-82. The assay for in vitro biological activity was performed as described in EXAMPLE 13. Antigen concentration of each conditioned medium was determined by ELISA as described in EXAMPLE 24. Table 14 shows specific activity of the mutants relative to that of the unaltered OCIF.

Table 14

mutants	activity
the unaltered OIF	++
OCIF-C19S	+
OCIF-C20S	±
OCIF-C21S	±
OCIF-C22S	+
OCIF-C23S	++
OCIF-DCR1	±
OCIF-DCR2	±
OCIF-DCR3	±
OCIF-DCR4	±
OCIF-DDD1	+
OCIF-DDD2	±
OCIF-CL	++
OCIF-CC	++
OCIF-CDD2	++
OCIF-CDD1	+
OCIF-CCR4	±
OCIF-CCR3	±
OCIF-CBst	++

OCIF-CSph	++
OCIF-CBsp	±
OCIF-CPst	±

++ indicates relative activity more than 50% of that of the unaltered OCIF + indicates relative activity between 10% and 50% ± indicates relative activity less than 10%, or production level too low to determine the accurate biological activity

vii) western blot analysis

Ten microliters of the final conditioned medium was used for western blot analysis. Ten microliters of the sample were mixed with 10 μl of SDS-PAGE sample buffer (0.5 M Tris-HCl, 20% glycerol, 4% SDS, 20 μg/ml bromo phenol blue, pH 6.8) boiled for 3 min. and subjected to a 10 % SDS polyacryl amide gel electrophoresis under non-reducing conditions. After the electrophoresis, the separated proteins were blotted to PVDF membrane (ProBlott^{R}, Perkin Elmer) using a semi-dry electroblotter (BIO-RAD). The membrane was incubated at 37℃ with horseradish peroxidase labeled anti-OCIF antibodies for 2 hr. After the membrane was washed, protein bands which react with the labeled antibodies were detected using ECL system (Amersham). Two protein bands with approximate molecular masses of 60kD and 120kD were detected for the unaltered OCIF. On the other hand, almost exclusively 60kD protein band was detected for OCIF-C23S, OCIF-CL and OCIF CC. Protein bands with an approximate masses of 40kD-50kD and 30kD-40kD were the major ones for OCIF-CDD2 and OCIF-CDD1, respectively. These results indicate that Cys at 379 is responsible for the

dimer formation, both the monomers and the dimers maintain the biological activity and a deletion of residues from Asp at 177 to Leu at 380 does not abolish the biological activity of OCIF (positions of the amino acid resare shown in SEQUENCE NO: 4).

EXAMPLE 23

Isolation of human genomic OCIF gene

i) Screening of a human genomic library

An amplified human placenta genomic library in Lambda FIX II vector purchased from STRATAGENE was screened for the gene encoding human OCIF using the human OCIF cDNA as a probe. Essentially, screening was done according to the instruction manual supplied with the genomic library. The basic protocols described in Molecular Cloning: A Laboratory Manual also were employed to manipulate phage, E. coli, and DNA .

The library was titered, and $1x10^6$ pfu of phage was mixed with XL1-Blue MRA host E. coli cells and plated on 20 plates (9 cm x 13 cm) with 9 ml per plate of top agarose. The plates were incubated overnight at 37℃. Filter plaque lifts were prepared using Hybond-N nylon membranes (Amersham). The membranes were processed by denaturation in a solution containing 1.5 M NaCl and 0.5 M NaOH for 1 minute at room temperature. The membranes were then neutralized by placing successively for one minute each in 1 M Tris-HCl (pH7.5) and a solution containing 1.5 M NaCl and 0.5 M Tris-HCl (pH 7.5). The membranes were then transferred onto a filter paper wet with 2xSSC. Phage DNA was fixed on the membranes with 1200 μ Joules of UV energy in STRATALINKER UV crosslinker 2400 (STRATAGENE) and the membranes were air dried. The membranes were immersed in Rapid Hybridization buffer (Amersham) and incubated for one hour at 65 ℃ before hybridization with ^{32}P-labeled cDNA probe in the same buffer overnight at 65℃. Screening probe was prepared by labeling the

OCIF cDNA with ^{32}P using the Megaprime DNA labeling system (Amersham). Approximately, $5x10^5$cpm probe was used for each ml of hybridization buffer. After the hybridization, the membranes were rinsed in 2xSSC for five minutes at room temperature. The membranes were then washed four times, 20 minutes each time, in 0.5xSSC containing 0.1 % SDS at 65 ℃. After the final wash, the membranes were dried and subjected to autoradiography at -80 ℃ with SUPER HR-H X-ray film (FUJI PFOTO FILM Co., Ltd.) and an intensifying screen. Upon examination of the autoradiograms, six positive signals were detected. Agar plugs were picked from the regions corresponded to these signals for phage purification. Each agar plug was soaked overnight in 0.5 ml of SM buffer containing 1% chloroform to extract phage. Each extract containing phage was diluted 1000 fold with SM buffer and an aliquot of 1 ml or 20 ml was mixed with host E. coli described above. The mixture was plated on agar plates with top agarose as described above. The plates were incubated overnight at 37 ℃, and filter lifts were prepared, prehybridized, hybridized, washed and autoradiographed as described above. This process of phage purification was applied to all six positive signals initially detected on the autoradiograms and was repeated until all phage plaques on agar plates hybridize with the cDNA probe. After purification, agar plugs of each phage isolate were soaked in SM buffer containing 1% chloroform and stored at 4 ℃. Six individual phage isolates were designated λOIF3, λOIF8, λOIF9, λOIF11, λOIF12 and λOIF17, respectively.

ii) Analysis of the genomic clones by restriction enzyme digestion and

Southern blot hybridization

DNA was prepared from each phage isolate by the plate lysate method as described in Molecular Cloning: A Laboratory Manual. DNA prepared from each phage was digested with restriction enzymes and the fragments derived from the digestion were separated on agarose gels. The fragments were then transferred to nylon membranes and subjected to Southern blot hybridization using OCIF cDNA as a probe. The results of the analysis revealed that the six phage isolates are individual clones. Among these fragments derived from the restriction enzyme digestion, those fragments which hybridized with the OCIF cDNA probe were subcloned into plasmid vectors and subjected to the nucleotide sequence analysis as described below.

iii) Subcloning restriction fragments derived from genomic clones into plasmid vectors and determination of the nucleotide sequence.

λOIF8 DNA was digested with restriction enzymes EcoRI and NotI, and the DNA fragments derived these from were separated on a 0.7% agarose gel. The 5.8 kilobase pairs (kb) EcoRI/NotI fragment was extracted from the gel using QIAEX II Gel Extraction Kit (QIAGEN) according to the procedure recommended by the manufacturer. The 5.8 kb EcoRI/NotI fragment was ligated with pBluescript II SK+ vector (STRATAGENE) which had been linearized with restriction enzymes EcoRI and NotI, using Ready-To-Go T4 DNA Ligase (Pharmacia) according to the procedure recommended by the manufacturer. Competent DH5 α E. coli cells (Amersham) were transformed with the recombinant plasmid and transformants were selected on L-plates containing 50 μg/ml of ampicillin.

A clone harboring the recombinant plasmid containing the 5.8 kb EcoRI/NotI fragment was isolated and this plasmid was termed pBSG8-5.8. pBSG8-5.8 was digested with HindIII and 0.9 kb of DNA fragment derived from this digestion was isolated in the same manner as described above. This 0.9 kb fragment was then cloned in pBluescript II SK- at the HindIII site as described above. This recombinant plasmid containing 0.9 kb HindIII fragment was denoted pBS8H0.9.

λOIF11 DNA was digested with EcoRI and 6 kb, 3.6 kb, 2.6 kb EcoRI fragments were isolated in the same manner as described above and cloned in pBluescript II SK+ vector at the EcoRI site as described above. These recombinant plasmids were termed pBSG11-6, pBSG11-3.6, and pBSG11-2.6, respectively. pBSG11-6 was digested with HindIII and the digest was applied on a 0.7 % agarose gel. Three fragments, 2.2 kb, 1.1 kb, and 1.05 kb in length, were extracted from the gel and cloned independently in pBluescript II SK- vector at the HindIII site in the same manner as described above. These recombinant plasmids were termed pBS6H2.2, pBS6 H1.1 and pBS6H1.05, respectively.

The nucleotide sequence of the cloned genomic DNA was determined using ABI Dyedeoxy Terminator Cycle Sequencing Ready Reaction Kit (PERKIN ELMER) and 373A DNA Sequencing system (Applied Biosystems). Plasmids pBSG8-5.8, pBS8H0.9, pBSG11-6, pBSG11-3.6, pBSG11-2.6, pBS6H2.2, pBS6H1.1 and pBS6H1.05 were prepared according to the alkaline-SDS procedure as described in Molecular Cloning: A Laboratory Manual and used as templates for the DNA sequence analysis. Nucleotide sequence of the human OCIF gene was presented in Sequence No 104 and Sequence No 105. The nucleotide sequence of the DNA,

between exon 1 and exon 2 was not entirely determined. There is a stretch of approximately 17 kb of nucleotides between the sequences given in sequence No. 104 and sequence No. 105.

EXAMPLE 24

Quantitation of OCIF by EIA

i) Preparation of anti-OCIF antibody

Male JW rabbits (Kitayama LABES Co.,LTD) weighing 2.5-3.0 kg were used for immunization for preparing antisera. Three male JW rabbits (Kitayama LABES Co., LTD) weighing 2.5-3.0 kg were used for immunization. For immunization, emulsion was prepared by mixing an equal volume of rOCIF (200 μg/ml) and complete Freund's adjuvant (Difco, Cat. 0638-60-7). The rabbits were immunized subcutaneously six times at the interval of one week with 1 ml of emulsion per injection. The rabbits were injected six times at the interval of seven days subcutaneously. Whole blood was obtained ten days after the final immunization and serum was separated. Antibody was purified from serum as follows. Antiserum was diluted two-fold with PBS. After adding ammonium sulfate at a final concentration of 40 w/v %, antiserum was allowed to stand at 4 ℃ for 1 hr.. Precipitate obtained by centrifugation at 8000 x g for 20 min. was dissolved in a small volume of PBS and was dialyzed against PBS. The resulting solution was loaded onto a Protein G-Sepharose column (Pharmacia). After washing with PBS, absorbed immunoglobulin G was eluted with 0.1 M glycine-HCL buffer (pH 3.0). Elutes were neutralized with 1.5 M Tris-HCL buffer (pH 8.7) immediately and were dialyzed against PBS. Protein

concentration was determined by absorbance at 280nm ($E^{1\%}$ 13.5).

Horseradish peroxidase labeled antibody was prepared using ImmunoPure Maleimide Activated Horseradish Peroxidase Kit (Pierce, Cat.31494). Briefly, one mg of IgG was incubated with 80 ug of N-succinimidyl-S-acetylthioacetate for 30 min. After deacetylation with 5 mg of hydroxylamine HCl, modified IgG was separeted by polyacrylamide desalting column. Protein pool mixed with one mg of maleimide activated horseradish peroxidase was incubated at room temperature for 1 hr.

ii) Quantitation of OCIF by sandwich EIA

Microtiter plates (Nunc MaxiSorp Immunoplate) were coated with rabbit anti-OCIF IgG by incubating 0.2 ug in 100 ul of 50 mM sodium bicarbonate buffer pH 9.6 at 4C overnight. After blocking the plates by incubating for 1 hour at 37℃ with 300 ul of 25% BlockAce/PBS (Snow Brand Milk Products), 100ul of samples were incubated for 2 hours at room temperature. After washing the plates three times with PBST (PBS containing 0.05% Tween20), 100 ul of 1:10000 diluted horseradish peroxidase labeled anti-OCIF IgG was added and incubated for 2 hours at room temperture. The amount of OCIF was determined by incubation with 100 ul of a substrate solution (TMB, ScyTek Lab.,Cat.TM4999) and measurement of the absorbance at 450 nm using an ImmunoReader (Nunc NJ2000). Purified recombinant OCIF was used as a standard protein and a typical standared curve was shown in Fig. 13.

EXAMPLE 25

Anti-OCIF monoclonal antibody

i) Preparation of hybridoma producing anti-OCIF monoclonal antibody.

OCIF was purified to homogeneity from culture medium of human fibroblasts, IMR-90 by the purification method described in Eample 11. Purified OCIF was dissolved in PBS at a concentration of 10 μg/100 μl. BALB/c mice were immunized by administrating this solution intraperitoneally three times every two weeks. In the first and the second immunizations, the emulsion composed of an equal volume of OCIF and Freund's complete adjuvant was administered. Three days after the final administration, the spleen was taken out, lymphocytes were isolated and fused with mouse myeloma p3x63-Ag8.653 cells according to the conventinal method using polyethyleneglycol. Then the fused cells were cultured in HAT medium to select hybridoma. Subsequently, to check whether the selected hybridomas produce anti-OCIF antibody, anti-OCIF antibody in each culture medium of hybridomas was determined by solid phase ELISA which was prepared by coating each well in 96-well immunoplates (Nunc) with 100μl of purified OCIF (10μg/ml in 0.1 M $NaHCO_3$) and by blocking each well with 50% BlockAce (Snow Brand Milk Products Co. Ltd.). The hybridoma clones secreting anti-OCIF antibody were established by cloning 3 - 5 times by limit dilution and by screening using the above solid phase ELISA. Among thus obtained hybridoma clones, several hybridoma clones with high production of anti-OCIF antibody were selected.

ii) Production of anti-OCIF monoclonal antibodies.

Each hybridoma clone secreting anti-OCIF antibody, which was obtained in

EXAMPLE 25-i), was transplanted intraperitoneally to mice given Pristane (Aldrich) at a cell density of 1 x 10^6 cells/mouse. The accumulated ascites was collected 10 - 14 days after the transplantation and the ascites containing anti-OCIF specific monoclonal antibody of the present invention was obtained. Purified antibodies were obtained by Affigel protein A Sepharose

chromatography (BioRad) according to the maufacturer's manual. That is, the ascites was diluted with equal volume of a binding buffer (BioRad) and applied to protein A column. The column was washed with a sufficient volume of the binding buffer and eluted with an elution buffer (BioRad). After neutralizing, the obtained eluate was dialyzed in water and subsequently lyophilized. The purity of the obtained antibody was analyzed by SDS/PAGE and a homogenous band with a molecular weight of about 150,000 was detected.

iii) Selection of monoclonal antibody having high affinity to OCIF

Each antibody obtained in EXAMPLE 25-ii) was dissolved in PBS and the concentration of protein in the solution was determined by the method of Lowry. Each antibody solution with the same concentration was prepared and then serially diluted with PBS. Monoclonal antibodies, which can recognize OCIF even at highly diluted solution, were selected by solid phase ELISA described in EXAMPLE 25-ii). Thus three monoclonal antibodies A1G5, E3H8 and D2F4 can be selected.

iv) Determination of class and subclass of antibodies

The class and subclass of the antibodies of the present invention obtained in EXAMPLE 25-iii) were analyzed using an immunoglobulin class and subclass analysis kit (Amersham). The procedure was carried out according to the protocol disclosed in the directions. The results were shown in Table 15. The antibodies of the present invention, E3H8, A1G5 and D2F4 belong to IgG_1, IgG_{2a} and IgG_{2b}, respectively.

Table 15

Analysis of class and subclass of the antibodies in the present invention.

Antibody	IgG_1	IgG_{2a}	IgG_{2b}	IgG_3	IgA	IgM	κ
A1G5	−	+	−	−	−	−	+
E3H8	+	−	−	−	−	−	+
D2F4	−	−	+	−	−	−	+

v) Determination of OCIF by ELISA

Three kinds of monoclonal antibodies, A1G5, E3H8 and D2F4, which were obtained in EXAMPLE 25-iv), were used as solid phase antibodies and enzyme-labeled antibodies, respectively. Sandwich ELISA was constructed by each combination of solid phase antibody and labeled antibody. The labeled antibody was prepared using Immuno Pure Maleimide Activated Horseradish Peroxidase Kit (Pierce, Cat. No. 31494). Each monoclonal antibody was

dissolved in 0.1 M $NaHCO_3$ at a concentration of 10 μg/ml, and 100 μl of the solution was added to each well in 96-well immunoplates (Nunc, MaxiSorp Cat. No. 442404) followed by allowing to stand at room temperature overnight. Subsequently, each well in the plates was blocked with 50% Blockace (Snow Brand Milk Products, Co., Ltd.) at room temperature for 50 minutes, and then was washed three times with PBS containing 0.1% Tween 20 (washing buffer).

A series of concentrations of OCIF was prepared by diluting OCIF with 1st reaction buffer (0.2 M Tris-HCl bufer, pH 7.4, containing 40% Blockace and 0.1% Tween 20). Each well in 96-well immunoplates was filled with 100μl of the prepared OCIF solution with each concentration, allowed to stand at 37 ℃ for 3 hours, and subsequently washed three times with the washing buffer. For dilution of POD-labeled antibody, 2nd reaction buffer (0.1 M Tris-HCl buffer, pH 7.4, containing 25% Blockace and 0.1% Tween 20) was used. POD-labeled antibody was diluted 400-fold with 2nd reaction buffer, and 100 μl of the diluted solution was added to each well in the immunoplates. Each imunoplate was allowed to stand at 37 ℃C for 2 hours, and subsequently washed three times with the washing buffer. After washing, 100 μl of a substrate solution (0.1 M citrate-phosphate buffer, pH 4.5, containing 0.4 mg/ml of o-phenylenediamine HCl and 0.006% H_2O_2) was added to each well in the immunoplates and the immunoplates were incubated at 37℃ for 15 min. The enzyme reaction was terminated by adding 50 μl of 6 N H_2SO_4 to each well. The optical density of each well was determined at 492 nm using an immunoreader (ImmunoReader NJ 2000, Nunc).

Using three kinds of monoclonal antibody in the present invention, each

combination of solid phase and POD-labeled antibodies leads to a accurate determination of OCIF. Each monoclonal antibody in the present invention was confirmed to recognize a different epitope of OCIF. A typical standard curve of OCIF using a combination of solid phase antibody, A1G5 and POD-labeled antibody, E3H8 was shown in Fig. 14.

vi) Determination of OCIF in human serum

Concentration of OCIF in five samples of normal human serum was determined using an EIA system described in EXAMPLE 25-v). The immunoplates were coated with A1G5 as described in EXAMPLE 25-v), and 50 μl of 1st. reaction buffer was added to each well in the immunoplates. Subsequently, 50μl of each human serum was added to each well in the immunoplates. The immnuoplates were incubated at 37℃ for 3 hours and then washed three times with the washing buffer. After washing, each well in the immunoplates was filled with 100μl of POD-E3H8 antibody diluted 400-fold with 2nd. reaction buffer and incubated at 37℃ for 2 hours. After washing the immunoplates three times with the washing buffer, 100 μl of the substrate solution described in EXAMPLE 25-v) was added to each well and incubated at 37℃ for 15 min. The enzyme reaction was terminated by adding 50 μl of 6 N H_2SO_4 to each well in the immunoplates. The optical density of each well was determined at 492 nm using an immunoreader (ImmunoReader NJ 2000, Nunc).

1st. reaction buffer containing the known amount of OCIF was treated in the same way and a standard curve of OCIF as shown in fig. 2 was obtained. Using the standard curve of OCIF, the amount of OCIF in human serum sample was

determined. The results were shown in Table 14.

Table 14

The amount of OCIF in normal human serum

Serum Sample	OCIF Concentration (ng/ml)
1	5. 0
2	2. 0
3	1. 0
4	3. 0
5	1. 5

EXAMPLE 26

Therapeutic effect on osteoporosis

(1) Method

Male Fischer rats, 6 weeks-old, were subjected to denervation of left forelimb. These rats were assigned to four groups(10 rats/group) and treated as follows ; group A, sham operated rats without administration ; group B, denervated rats with intravenous administration of vehicle ; group C, denervated rats administered OCIF intravenously at a dose of 5 μg/kg twice a day ; group D, denervated rats administered OCIF intravenously at a dose of 50 μg/kg twice a day. After denervation, OCIF was administered daily for 14 days. After 2 weeks treatment, the animals were sacrificed and their forelimbs were dissected. Thereafter bones were tested for mechanical

strength.

(2) Results

Decrease of bone strength was observed in the animals of control groups as compared to those animals of the normal groups while bone strength was increase in the groups of animal received 50 mg of OCIF per kg body weight.

Industrial availability

The present invention provides both a novel protein which inhibits formation of osteoclasts and a efficient procedure to produce the protein. The protein of the present invention has an activity to inhibit formation of osteoclasts. The protein will be useful for the treatment of many diseases accompanying bone loss, such as osteoporosis, and as an antigen to be used for the immunological diagnosis of such diseases.

Referring to the deposited the microorgainsm

Name and Address of the Depositary Authority

Name: National Institute of Bioscience and Human-Technology
Agency of Industrial Science and Technology
Ministry of International Trade and Industry

Address: 1-3, Higashi 1-chome, Tsukuba-shi, Ibaraki-ken
305, JAPAN

Deposited date: June 21, 1995

(It was transferred from Bikkoken No. P-14998, which was deposited on June 21, 1995. Transferred date: October 25, 1995)

Acession Number: FERM BP-5267

CLAIMS

1. An osteoclastogenesis inhibitory factor protein comprising the following properties:

(a) molecular weights as determined by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) of approximately 60 kD under reducing conditions, and
approximately 60 kD and 120 kD under non-reducing conditions;

(b) high affinity to cation-exchange resins and heparin derivatized substrates;

(c) inhibition activity: inhibits osteoclast differentiation or maturation, wherein the inhibition activity is decreased by heating at about 70°C for about 10 min. or at about 56°C for about 30 min., and wherein said activity is lost by heating at about 90°C for about 10 min.; and

(d) internal amino acid sequences substantially in accordance with Seq. ID Nos. 1, 2 and 3.

2. The protein of claim 1 comprising the N-terminal amino acid sequences provided in Seq. ID No. 7.

3. The protein of claim 1 which is derived from human fibroblasts.

4. A method of producing an osteoclastogenesis inhibitory factor protein comprising the steps of
cultivating human fibroblast cells;
forming a lysate of said fibroblast cells; and
separating said factor from said fibroblast cell lysate by a combination of ion-exchange, affinity, and reverse phase chromatography.

5. The method of claim 4 further comprising the step of cultivating the human fibroblasts on alumina ceramic pieces.

6. A protein comprising an amino acid sequence as provided in Seq. ID No. 4.

7. cDNAs encoding an amino acid sequence as provided in Seq. ID No. 4.

8. cDNA comprising a nucleotide sequence as provided in Seq. ID No. 6.

9. cDNAs that hybridize to a cDNA as provided in Seq. ID No. 6 under moderately stringent conditions.

10. A protein expressed from cDNA encoding an amino acid sequence as provided in Seq. ID No. 4.

11. A protein having a biological activity to inhibit osteoclast differentiation or maturation, said protein having an amino acid sequence expressed from a cDNA sharing at least about 80% sequence identity with the amino acid sequence provided in Seq. ID No. 4.

12. A recombinant protein which inhibits osteoclast differentiation or maturation expressed from a cDNA encoding an amino acid sequence as provided in Seq. ID No. 4; said protein comprising the following properties:

(a) molecular weights as determined by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) of approximately 60 kD under reducing conditions, and
approximately 60 kD and 120 kD under non-reducing conditions;

(b) high affinity to cation-exchange resins and heparin derivatized substrates;

(c) inhibitory activity: inhibits osteoclast differentiation or maturation, wherein said activity is decreased by heating at about 70°C for about 10 min. or at about 56°C for about 30 min., and
wherein said activity is lost by heating at about 90°C for about 10 min.; and

(d) an internal amino acid sequence as provided in Seq. ID Nos. 1-3.

13. The protein of claim 10 produced by gene engineering using mammalian cells as host cells.

14. The protein of claim 13 wherein said mammalian cells are 293/EBNA cells or CHO cells.

15. A cDNA comprising a nucleotide sequence as provided in Seq. ID No. 8.

16. A protein encoded by a cDNA having a nucleotide sequence as provided in Seq. ID No. 8.

17. cDNAs encoding amino acid sequence as provided in Seq. ID No. 9.

18. A cDNA comprising a nucleotide sequence as provided in Seq. ID No. 10.

19. A protein encoded by a cDNA comprising a nucleotide sequence as provided in Seq. ID No. 10.

20. cDNAs encoding an amino acid sequence as provided in Seq. ID No. 11.

21. A cDNA comprising a nucleotide sequence as provided in Seq. ID No. 12.

22. A protein encoded by a cDNA having a nucleotide sequence as provided in Seq. ID No. 12.

23. cDNAs encoding an amino acid sequence as provided in Seq. ID No. 13.

24. A cDNA comprising a nucleotide sequence as provided in Seq. ID No. 14.

25. A protein encoded by a cDNA having a nucleotide sequence as provided in Seq. ID No. 14.

26. cDNAs encoding an amino acid sequence as provided in Seq. ID No. 15.

27 An antibody having specific affinity to the osteoclastogenesis inhibitory factor protein of claim 1.

28. The antibody of claim 27 that is polyclonal.

29. The antibody of claim 27 that is monoclonal.

30. The monoclonal antibody of claim 29 comprising the following properties: a molecular weight of about 150,000, and of subclass IgG_1, IgG_{2a}, or IgG_{2b}.

31. A method for determining the concentration of an osteoclastogenesis inhibitory factor protein comprising contacting a sample suspected of containing said protein with an antibody of claim 27, 28, 29 or 30 under conditions sufficient to induce formation of protein-antibody conjugates, and detecting the amount of protein-antibody conjugates formed.

188PAC3999/1.398800

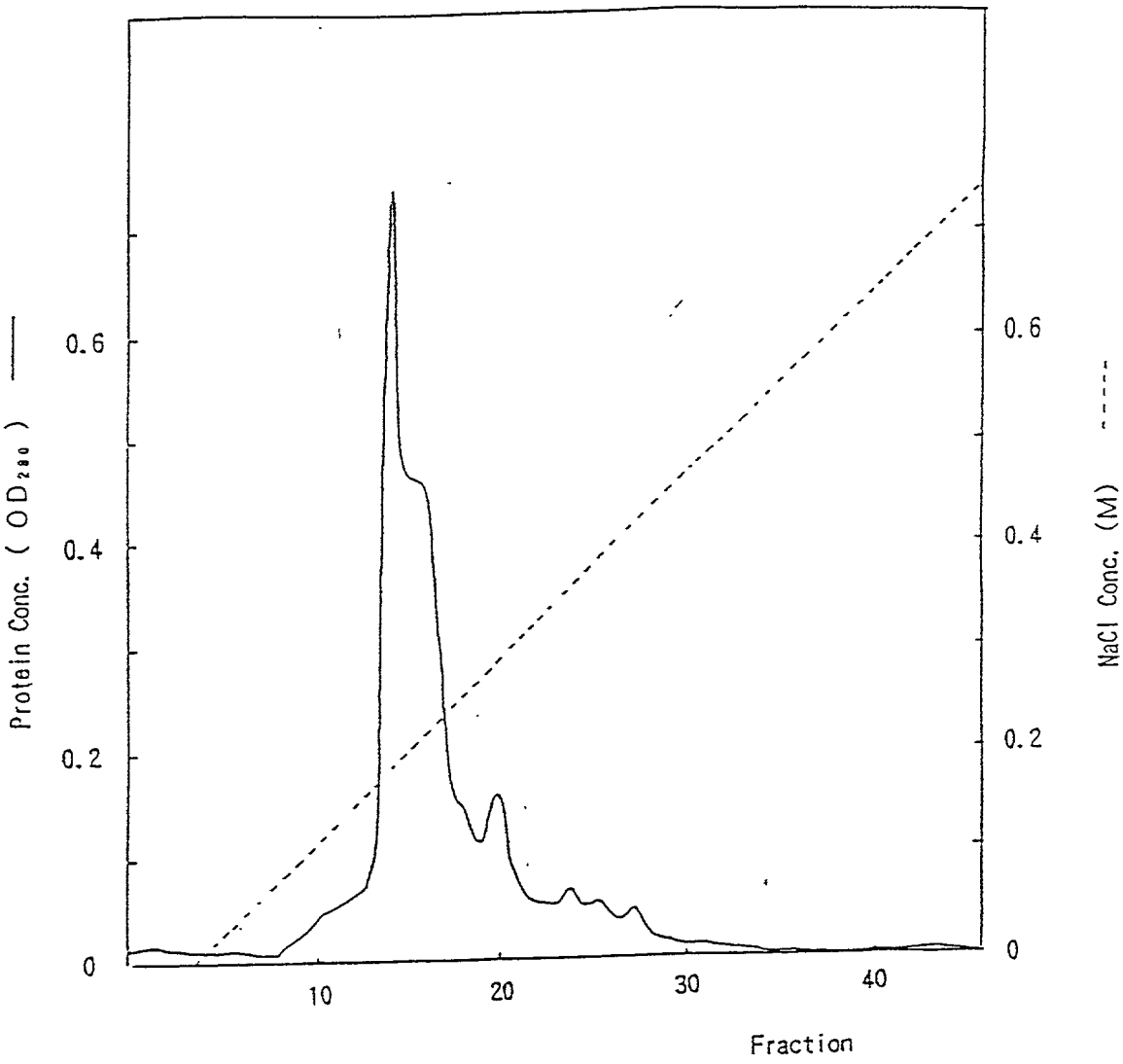
Abstract

A protein which inhibits osteoclast differentiation and/or maturation and a method of production of the protein. The protein is produced by human embryonic lung fibroblasts and has molecular weight of about 60 kD and about 120 kD under non-reducing conditions and about 60 kD under reducing conditions on SDS-polyacrylamide gel electrophoresis, respectively.

The protein can be isolated and purified from culture medium of the said fibroblasts. Furthermore, the protein can be produced by gene engineering.

The present invention includes cDNA for producing the protein by gene engineering, antibodies having specific affinity to the protein or a method for determination of the protein concentration using the antibodies.

Fig. 1



	Dilution			
OCIF Activity	1/100	−	++	++	−
	1/500	−	++	++	−

Fig. 2

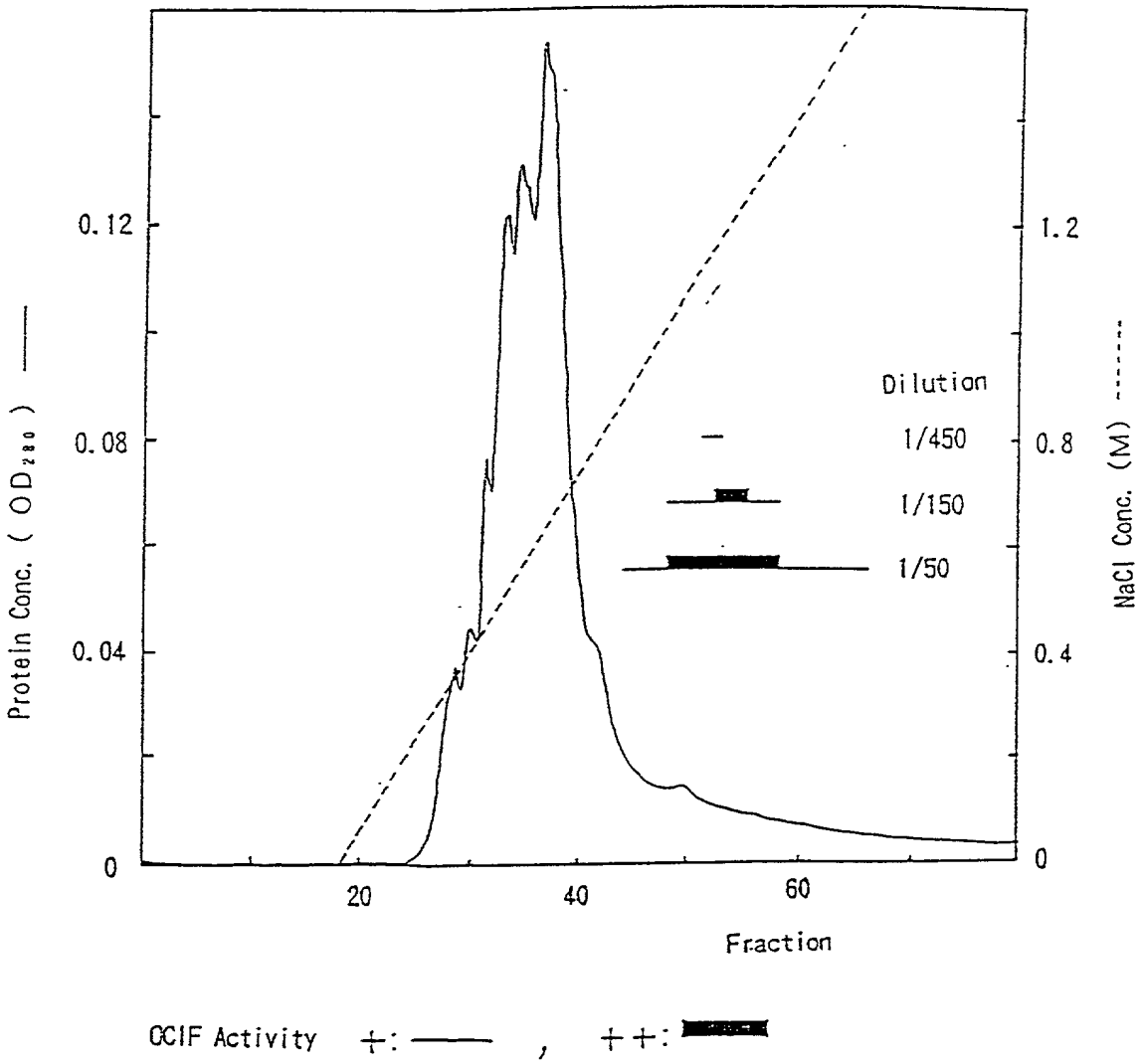

0.12
0.08
0.04
0
Protein Conc. (OD_{280}) ——
1.2
0.8
0.4
0
NaCl Conc. (M) - - - - - -
20
40
60
Fraction
Dilution
1/450
1/150
1/50
CCIF Activity +: —— , ++:

Fig. 3

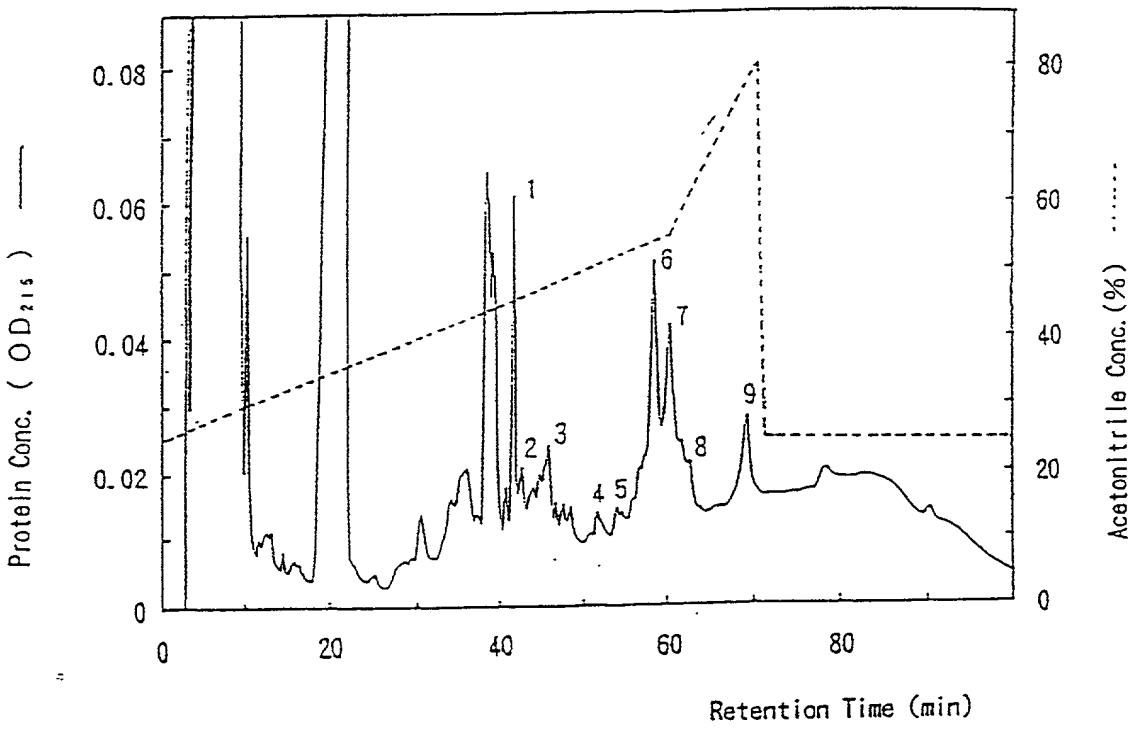
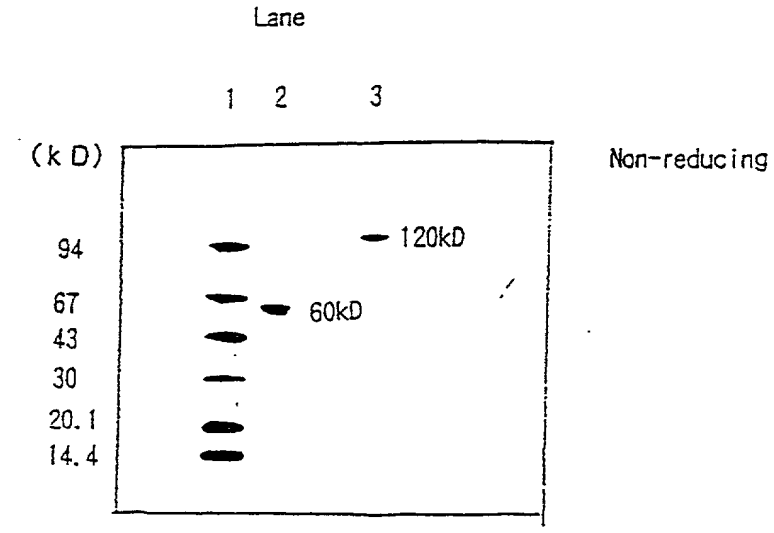

Protein Conc. (OD215) ——
Acetonitrile Conc.(%) .....
0.08
0.06
0.04
0.02
0
80
60
40
20
0
0
20
40
60
80
Retention Time (min)
1
2
3
4
5
6
7
8
9

Fig. 4


Lane
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(k D)
94
67
43
30
20.1
14.4
120kD
60kD
Non-reducing

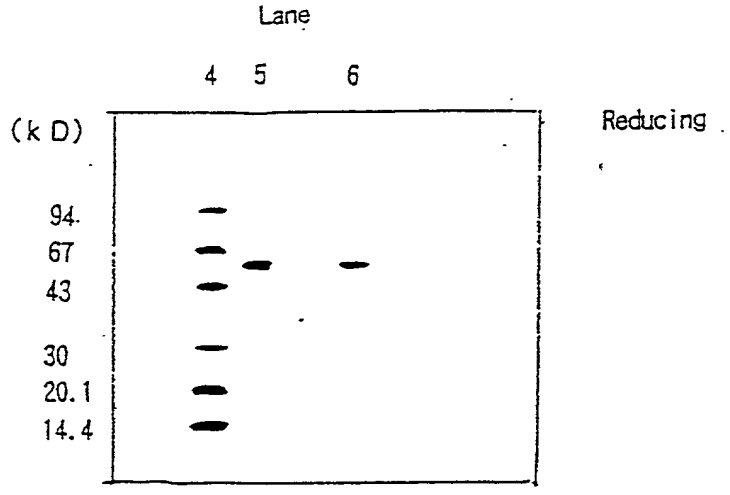

Lane
4 5 6
(k D)
94
67
43
30
20.1
14.4
Reducing

Fig.5

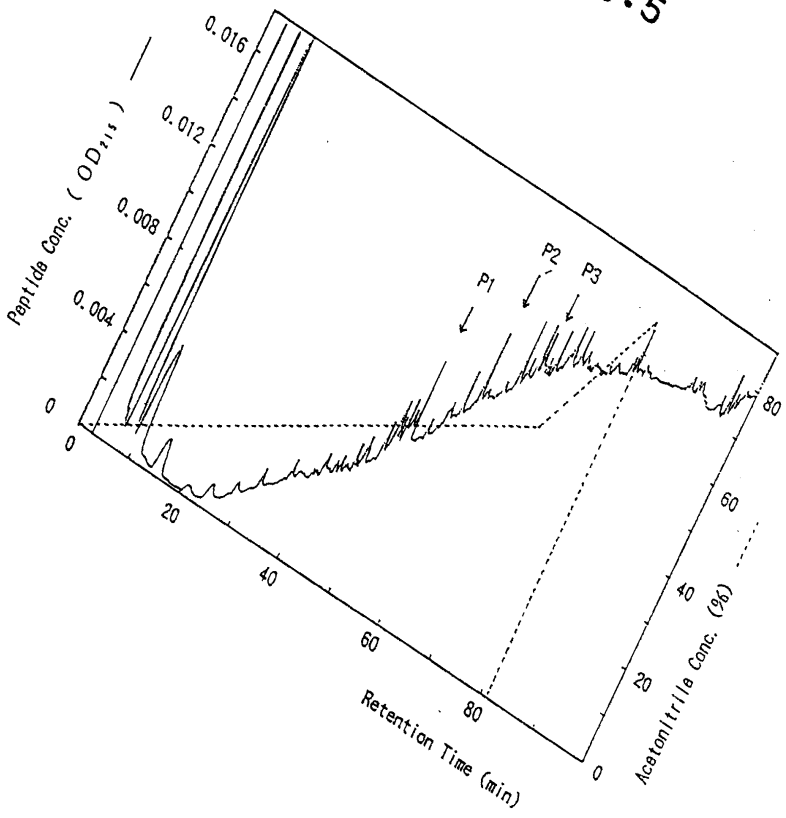

Peptide Conc. (OD215)
0.016
0.012
0.008
0.004
0
P1
P2
P3
0
20
40
60
80
Retention Time (min)
0
20
40
60
80
Acetonitrile Conc. (%)

Fig. 6

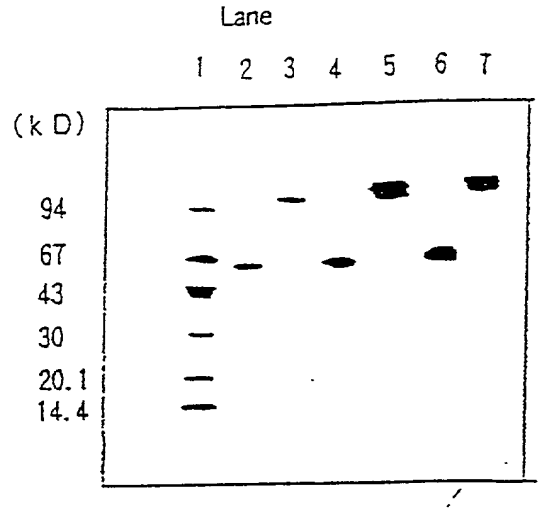


Fig. 7

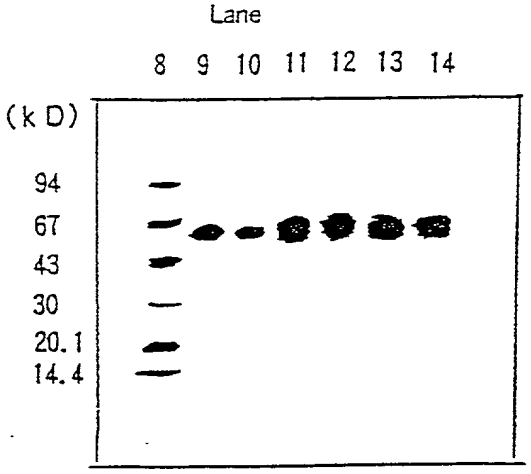


Fig.8

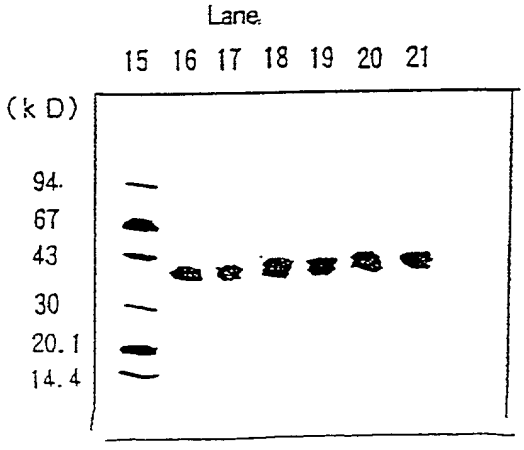


Fig. 9

```
1
MNNLLCCALVFLDISIKWTTQETFPPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKT (OCIF1)
************************************************************
MNNLLCCALVFLDISIKWTTQETFPPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKT (OCIF2)
1

61
VCAPCPDHYYTDSWHTSDECLYCSPVCKELQYVKQECNRTHNRVCECKEGRYLEIEFCLK (OCIF1)
*****************************       ************************
VCAPCPDHYYTDSWHTSDECLYCSPVCKE-------CNRTHNRVCECKEGRYLEIEFCLK (OCIF2)
61

121
HRSCPPGFGVVQAGTPERNTVCKRCPDGFFSNETSSKAPCRKHTNCSVFGLLLTQKGNAT (OCIF1)
************************************************************
HRSCPPGFGVVQAGTPERNTVCKRCPDGFFSNETSSKAPCRKHTNCSVFGLLLTQKGNAT (OCIF2)
114

181
HDNICSGNSESTQKCGIDVTLCEEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERI (OCIF1)
************************************************************
HDNICSGNSESTQKCGIDVTLCEEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERI (OCIF2)
174

241
KRQHSSQEQTFQLLKLWKHQNKDQDIVKKIIQDIDLCENSVQRHIGHANLTFEQLRSLME (OCIF1)
************************************************************
KRQHSSQEQTFQLLKLWKHQNKDQDIVKKIIQDIDLCENSVQRHIGHANLTFEQLRSLME (OCIF2)
234

301
SLPGKKVGAEDIEKTIKACKPSDQILKLLSLWRIKNGDQDTLKGLMHALKHSKTYHFPKT (OCIF1)
************************************************************
SLPGKKVGAEDIEKTIKACKPSDQILKLLSLWRIKNGDQDTLKGLMHALKHSKTYHFPKT (OCIF2)
294

361
VTQSLKKTIRFLHSFTMYKLYQKLFLEMIGNQVQSVKISCL (OCIF1)
****************************************
VTQSLKKTIRFLHSFTMYKLYQKLFLEMIGNQVQSVKISCL (OCIF2)
354
```

Fig. 10

```
1
MNNLLCCALVFLDISIKWTTQETFPPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKT (OCIF1)
** *********************************************************
MNKLLCCALVFLDISIKWTTQETFPPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKT (OCIF3)
1

61
VCAPCPDHYYTDSWHTSDECLYCSPVCKELQYVKQECNRTHNRVCECKEGRYLEIEFCLK (OCIF1)
************************************************************
VCAPCPDHYYTDSWHTSDECLYCSPVCKELQYVKQECNRTHNRVCECKEGRYLEIEFCLK (OCIF3)
61

121
HRSCPPGFGVVQAGTPERNTVCKRCPDGFFSNETSSKAPCRKHTNCSVFGLLLTQKGNAT (OCIF1)
************************************************************
HRSCPPGFGVVQAGTPERNTVCKRCPDGFFSNETSSKAPCRKHTNCSVFGLLLTQKGNAT (OCIF3)
121

181
HDNICSGNSESTQKCGIDVTLCEEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERI (OCIF1)
************************************************************
HDNICSGNSESTQKCGIDVTLCEEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERI (OCIF3)
181

241
KRQHSSQEQTFQLLKLWKHQNKDQDIVKKIIQDIDLCENSVQRHIGHANLTFEQLRSLME (OCIF1)
**************************************************
KRQHSSQEQTFQLLKLWKHQNKDQDIVKKIIQDIDLCENSVQRHIGHANLS--------- (OCIF3)
241

301
SLPGKKVGAEDIEKTIKACKPSDQILKLLSLWRIKNGDQDTLKGLMHALKHSKTYHFPKT (OCIF1)
                              ******************************
------------------------------LWRIKNGDQDTLKGLMHALKHSKTYHFPKT (OCIF3)
                              292

361
VTQSLKKTIRFLHSFTMYKLYQKLFLEMIGNQVQSVKISCL  (OCIF1)
*****************************************
VTQSLKKTIRFLHSFTMYKLYQKLFLEMIGNQVQSVKISCL  (OCIF3)
322
```

Fig. 11

```
1
MNNLLCCALVFLDISIKWTTQETFPPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKT (OCIF1)
** **** **************************************************
MNKLLCCSLVFLDISIKWTTQETFPPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKT (OCIF4)
1

61
VCAPCPDHYYTDSWHTSDECLYCSPVCKELQYVKQECNRTHNRVCECKEGRYLEIEFCLK (OCIF1)
************************************************************
VCAPCPDHYYTDSWHTSDECLYCSPVCKELQYVKQECNRTHNRVCECKEGRYLEIEFCLK (OCIF4)
61

121
HRSCPPGFGVVQAGTPERNTVCKRCPDGFFSNETSSKAPCRKHTNCSVFGLLLTQKGNAT (OCIF1)
***************
HRSCPPGFGVVQAGTCQCAAKLIRIMQSQIVVTV                            (OCIF4)
121
```

Fig. 12

```
1
MNNLLCCALVFLDISIKWTTQETFPPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKT (OCIF1)
** ************************************************************
MNKLLCCALVFLDISIKWTTQETFPPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKT (OCIF5)
1

61
VCAPCPDHYYTDSWHTSDECLYCSPVCKELQYVKQECNRTHNRVCECKEGRYLEIEFCLK (OCIF1)
************************************************************
VCAPCPDHYYTDSWHTSDECLYCSPVCKELQYVKQECNRTHNRVCECKEGRYLEIEFCLK (OCIF5)
61

121
HRSCPPGFGVVQAGTPERNTVCKRCPDGFFSNETSSKAPCRKHTNCSVFGLLLTQKGNAT (OCIF1)
**************   *
HRSCPPGFGVVQAGCRRRPKPQICI                                     (OCIF5)
121
```

Fig. 13

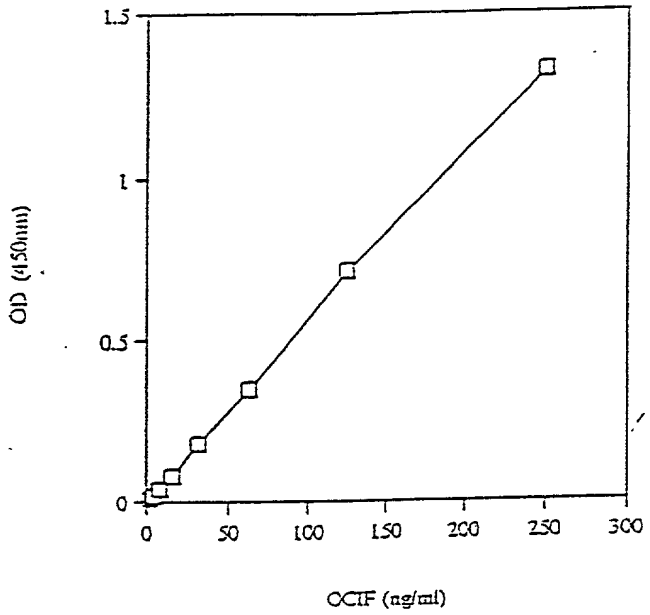

1.5
1
0.5
0
OD (450nm)
0
50
100
150
200
250
300
OCIF (ng/ml)

Fig. 14

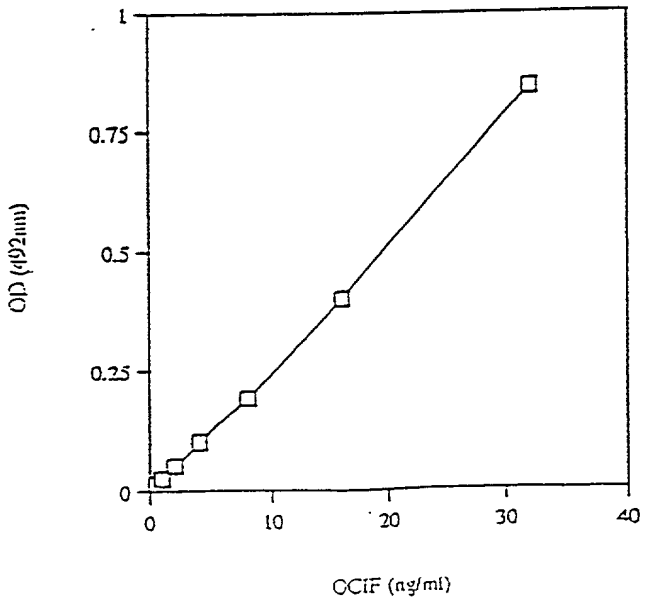
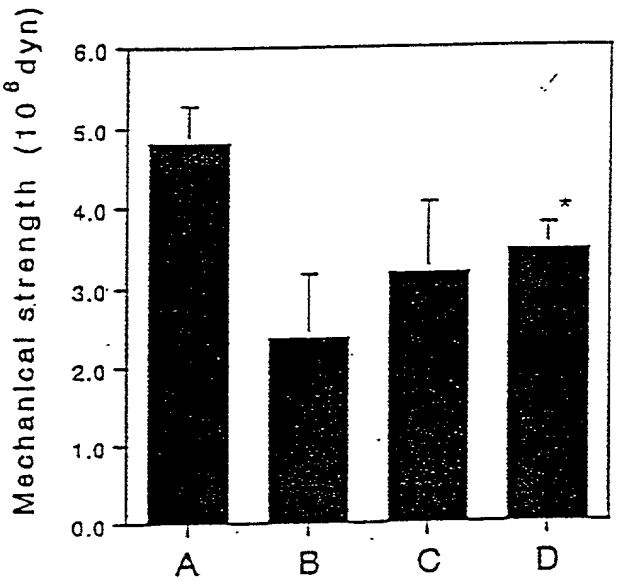

1
0.75
0.5
0.25
0
OD (492nm)
0
10
20
30
40
OCIF (ng/ml)

Fig. 15



A : Normal rat
B : Denerved rat + Vehicle
C : Denerved rat + OCIF 10μg/kg/day
C : Denerved rat + OCIF 100μg/kg/day

EXPRESS MAIL MAILING LABEL
No. EM601204925US

PATENT
Atty. Docket No. FJN-060
(3999/63)

COPY

COMBINED DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

(Original, Design, National Stage of PCT, Supplemental, Divisional, Continuation or CIP)

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name, and I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

NOVEL PROTEINS AND METHODS FOR PRODUCING THE PROTEINS

the specification of which (check one):

☒ is attached hereto.

☐ was filed on _____ as Application Serial No. 0_____/_____ or

☐ was described and claimed in PCT International Application No. _____ filed on _____ and as amended under PCT Article 19 on _____ (if any).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims as amended by any amendment referred to herein.

I acknowledge the continuing duty to disclose information which is material to the examination of this application in accordance with 37 C.F.R. §1.56.

PRIORITY CLAIM

☐ A. I hereby claim benefit under 35 U.S.C. 119(e) of United States Provisional Application No. ___, filed on _____.

☒ B. I hereby claim foreign priority benefits under 35 U.S.C. §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and I have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

☐ no such applications have been filed.

☒ such applications have been filed as follows:

EARLIEST FOREIGN APPLICATION(S), IF ANY FILED WITHIN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

Country	Application Number	Date of Filing (mo., day, year)	Priority Claimed Under 35 USC 119
			☐YES NO ☐

ALL FOREIGN APPLICATION(S), IF ANY FILED MORE THAN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

Country	Application Number	Date of Filing (mo., day, year)	Priority Claimed Under 37 USC 119
Japan	54977/1995	Feb. 20, 1995	☒YES NO ☐
Japan	207508/1995	July 21, 1995	☒YES NO ☐

☒ C. I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose material information as defined in 37 C.F.R. §1.56 which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application.

PRIOR U.S. NON-PROVISIONAL APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 USC §120:

U.S. APPLICATIONS	U.S. FILING DATE	STATUS
PCT/JP96/00374	Feb. 20, 1996	Pending
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, aband.)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, aband.)

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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EXPRESS MAIL MAILING LABEL

No. EM 601204925US

PATENT

Attorney Docket No. FJN-060DV2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S):	Goto et al.		
SERIAL NO.:	Not yet assigned	GROUP NO.:	Not yet assigned
FILED:	Herewith	EXAMINER:	Not yet assigned
TITLE:	NOVEL PROTEINS AND METHODS FOR PRODUCING THE PROTEINS		

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Respectfully submitted,

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(iii) NUMBER OF SEQUENCES: 108

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(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: JP 54977/1995
(B) FILING DATE: 20-FEB-1995

(vii) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: JP 207508/1995
(B) FILING DATE: 21-JUL-1995

(vii) PRIOR APPLICATION DATA:
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(B) FILING DATE: 20-FEB-1996

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(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "(an internal amino acid sequence of the protein)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Xaa Tyr His Phe Pro Lys
1 5

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..14
(D) OTHER INFORMATION: /note= "(an internal amino acid sequence of the protein)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Xaa Gln His Ser Xaa Gln Glu Gln Thr Phe Gln Leu Xaa Lys
1 5 10

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..12
(D) OTHER INFORMATION: /note= "(an internal amino acid sequence of the protein)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Xaa Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys
1 5 10

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 380 amino acids

(B) TYPE:amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..380
(D) OTHER INFORMATION: /note= "(OCIF protein without signal peptide)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```
Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp Glu Glu Thr Ser His
1               5                  10                  15

Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr Tyr Leu Lys Gln His
            20                  25                  30

Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro Cys Pro Asp His Tyr
        35                  40                  45

Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys Leu Tyr Cys Ser Pro
    50                  55                  60

Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu Cys Asn Arg Thr His
65                  70                  75                  80

Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr Leu Glu Ile Glu Phe
                85                  90                  95

Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala
            100                 105                 110

Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg Cys Pro Asp Gly Phe
        115                 120                 125

Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn
    130                 135                 140

Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys Gly Asn Ala Thr His
145                 150                 155                 160

Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile
                165                 170                 175

Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr
            180                 185                 190

Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val Asp Asn Leu Pro Gly
        195                 200                 205

Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile Lys Arg Gln His Ser
    210                 215                 220

Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu Trp Lys His Gln Asn
225                 230                 235                 240

Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys
                245                 250                 255

Glu Asn Ser Val Gln Arg His Ile Gly His Ala Asn Leu Thr Phe Glu
            260                 265                 270

Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly Lys Lys Val Gly Ala
```

275 280 5

Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys Pro Ser Asp Gln Ile
290 295 300

Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr
305 310 315 320

Leu Lys Gly Leu Met His Ala Leu Lys His Ser Lys Thr Tyr His Phe
325 330 335

Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr Ile Arg Phe Leu His
340 345 350

Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile
355 360 365

Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys Leu
370 375 380

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 401 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..380
(D) OTHER INFORMATION: /note= "(OCIF protein)"

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0
(D) OTHER INFORMATION: /note= "(signal peptide)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20 -15 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5 1 5 10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
15 20 25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60 65 70 75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
80 85 90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
95 100 105

```
Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
    125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
                160                 165                 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
            175                 180                 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
        190                 195                 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
    205                 210                 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220                 225                 230                 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
                240                 245                 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
            255                 260                 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
        270                 275                 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
    285                 290                 295

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300                 305                 310                 315

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
                320                 325                 330

Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
            335                 340                 345

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
        350                 355                 360

Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys
    365                 370                 375

Leu
380
```

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1206 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1206

(D) OTHER INFORMATION: /note= "(OCIF)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCTG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCATGCAAA 960

CCCAGTGACC AGATCCTGAA GCTGCTCAGT TTGTGGCGAA TAAAAAATGG CGACCAAGAC 1020

ACCTTGAAGG GCCTAATGCA CGCACTAAAG CACTCAAAGA CGTACCACTT TCCCAAAACT 1080

GTCACTCAGA GTCTAAAGAA GACCATCAGG TTCCTTCACA GCTTCACAAT GTACAAATTG 1140

TATCAGAAGT TATTTTTAGA AATGATAGGT AACCAGGTCC AATCAGTAAA AATAAGCTGC 1200

TTATAA 1206

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..15
(D) OTHER INFORMATION: /note= "(a N-terminal amino acid sequence of the protein)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp Glu Glu Thr Ser

1 5 10 15

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1185 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1185
(D) OTHER INFORMATION: /note= "(OCIF2)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGTGC AATCGCACCC ACAACCGCGT GTGCGAATGC 300

AAGGAAGGGC GCTACCTTGA GATAGAGTTC TGCTTGAAAC ATAGGAGCTG CCCTCCTGGA 360

TTTGGAGTGG TGCAAGCTGG AACCCCAGAG CGAAATACAG TTTGCAAAAG ATGTCCAGAT 420

GGGTTCTTCT CAAATGAGAC GTCATCTAAA GCACCCTGTA GAAAACACAC AAATTGCAGT 480

GTCTTTGGTC TCCTGCTAAC TCAGAAAGGA AATGCAACAC ACGACAACAT ATGTTCCGGA 540

AACAGTGAAT CAACTCAAAA ATGTGGAATA GATGTTACCC TGTGTGAGGA GGCATTCTTC 600

AGGTTTGCTG TTCCTACAAA GTTTACGCCT AACTGGCTTA GTGTCTTGGT AGACAATTTG 660

CCTGGCACCA AAGTAAACGC AGAGAGTGTA GAGAGGATAA AACGGCAACA CAGCTCACAA 720

GAACAGACTT TCCAGCTGCT GAAGTTATGG AAACATCAAA ACAAAGACCA AGATATAGTC 780

AAGAAGATCA TCCAAGATAT TGACCTCTGT GAAAACAGCG TGCAGCGGCA CATTGGACAT 840

GCTAACCTCA CCTTCGAGCA GCTTCGTAGC TTGATGGAAA GCTTACCGGG AAAGAAAGTG 900

GGAGCAGAAG ACATTGAAAA AACAATAAAG GCATGCAAAC CCAGTGACCA GATCCTGAAG 960

CTGCTCAGTT TGTGGCGAAT AAAAAATGGC GACCAAGACA CCTTGAAGGG CCTAATGCAC 1020

GCACTAAAGC ACTCAAAGAC GTACCACTTT CCCAAAACTG TCACTCAGAG TCTAAAGAAG 1080

ACCATCAGGT TCCTTCACAG CTTCACAATG TACAAATTGT ATCAGAAGTT ATTTTTAGAA 1140

ATGATAGGTA ACCAGGTCCA ATCAGTAAAA ATAAGCTGCT TATAA 1185

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 394 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..373
(D) OTHER INFORMATION: /note= "(OCIF2)"

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1               5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Cys Asn Arg Thr His Asn Arg
60                  65                  70                  75

Val Cys Glu Cys Lys Glu Gly Arg Tyr Leu Glu Ile Glu Phe Cys Leu
                80                  85                  90

Lys His Arg Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala Gly Thr
            95                  100                 105

Pro Glu Arg Asn Thr Val Cys Lys Arg Cys Pro Asp Gly Phe Phe Ser
        110                 115                 120

Asn Glu Thr Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn Cys Ser
    125                 130                 135

Val Phe Gly Leu Leu Leu Thr Gln Lys Gly Asn Ala Thr His Asp Asn
140                 145                 150                 155

Ile Cys Ser Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile Asp Val
                160                 165                 170

Thr Leu Cys Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr Lys Phe
            175                 180                 185

Thr Pro Asn Trp Leu Ser Val Leu Val Asp Asn Leu Pro Gly Thr Lys
        190                 195                 200

Val Asn Ala Glu Ser Val Glu Arg Ile Lys Arg Gln His Ser Ser Gln
    205                 210                 215

Glu Gln Thr Phe Gln Leu Leu Lys Leu Trp Lys His Gln Asn Lys Asp
220                 225                 230                 235

Gln Asp Ile Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys Glu Asn
                240                 245                 250

Ser Val Gln Arg His Ile Gly His Ala Asn Leu Thr Phe Glu Gln Leu
```

```
                25                  260                 265

Arg Ser Leu Met Glu Ser Leu Pro Gly Lys Lys Val Gly Ala Glu Asp
        270                 275                 280

Ile Glu Lys Thr Ile Lys Ala Cys Lys Pro Ser Asp Gln Ile Leu Lys
    285                 290                 295

Leu Leu Ser Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu Lys
300                 305                 310                 315

Gly Leu Met His Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro Lys
                320                 325                 330

Thr Val Thr Gln Ser Leu Lys Lys Thr Ile Arg Phe Leu His Ser Phe
            335                 340                 345

Thr Met Tyr Lys Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Gly Asn
        350                 355                 360

Gln Val Gln Ser Val Lys Ile Ser Cys Leu
    365                 370
```

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1089 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1089
(D) OTHER INFORMATION: /note= "(OCIF3)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

```
ATGAACAAGT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC      60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG     120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC     180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT     240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC     300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA     360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA     420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT     480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA     540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC     600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT     660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA     720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA     780
```

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCGA TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC AGTTTGTGGC GAATAAAAAA TGGCGACCAA 900

GACACCTTGA AGGGCCTAAT GCACGCACTA AAGCACTCAA AGACGTACCA CTTTCCCAAA 960

ACTGTCACTC AGAGTCTAAA GAAGACCATC AGGTTCCTTC ACAGCTTCAC AATGTACAAA 1020

TTGTATCAGA AGTTATTTTT AGAAATGATA GGTAACCAGG TCCAATCAGT AAAAATAAGC 1080

TGCTTATAA 1089

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 362 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..341
(D) OTHER INFORMATION: /note= "(OCIF3)"

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

```
Met Asn Lys Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1               5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
    125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155
```

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
160 165 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
175 180 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
190 195 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
205 210 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220 225 230 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
240 245 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
255 260 265

Asn Leu Ser Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu Lys
270 275 280

Gly Leu Met His Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro Lys
285 290 295

Thr Val Thr Gln Ser Leu Lys Lys Thr Ile Arg Phe Leu His Ser Phe
300 305 310 315

Thr Met Tyr Lys Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Gly Asn
320 325 330

Gln Val Gln Ser Val Lys Ile Ser Cys Leu
335 340

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 465 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..465
(D) OTHER INFORMATION: /note= "(OCIF4)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

ATGAACAAGT TGCTGTGCTG CTCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GTACGTGTCA ATGTGCAGCA 420

AAATTAATTA GGATCATGCA AAGTCAGATA GTTGTGACAG TTTAG 465

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 154 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..133
(D) OTHER INFORMATION: /note= "(OCIF4)"

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

```
Met Asn Lys Leu Leu Cys Cys Ser Leu Val Phe Leu Asp Ile Ser Ile
-20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Cys Gln Cys Ala Ala Lys Leu Ile Arg
        110                 115                 120

Ile Met Gln Ser Gln Ile Val Val Thr Val
    125                 130
```

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 438 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

(A) NAME/. .: -
(B) LOCATION: 1..438
(D) OTHER INFORMATION: /note= "(OCIF5)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

ATGAACAAGT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GATGCAGGAG AAGACCCAAG 420

CCACAGATAT GTATCTGA 438

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 145 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..124
(D) OTHER INFORMATION: /note= "(OCIF5)"

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Met Asn Lys Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20 -15 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5 1 5 10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
15 20 25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60 65 70 75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
80 85 90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe

95 100 105

Gly Val Val Gln Ala Gly Cys Arg Arg Arg Pro Lys Pro Gln Ile Cys
110 115 120

Ile

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer T3)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

AATTAACCCT CACTAAAGGG 20

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..22
(D) OTHER INFORMATION: /note= "synthetic DNA (primer T7)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

GTAATACGAC TCACTATAGG GC 22

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF1)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

ACATCAAAAC AAAGACCAAG 20

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF2)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

TCTTGGTCTT TGTTTTGATG 20

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF3)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

TTATTCGCCA CAAACTGAGC 20

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF4)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

TTGTGAAGCT GTGAAGGAAC 20

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF5)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

GCTCAGTTTG TGGCGAATAA 20

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF6)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

GTGGGAGCAG AAGACATTGA 20

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF7)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

AATGAACAAC TTGCTGTGCT 20

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF8)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

TGACAAATGT CCTCCTGGTA 20

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF9)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

AGGTAGGTAC CAGGAGGACA 20

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF10)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

GAGCTGCCCT CCTGGATTTG 20

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF11)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

CAAACTGTAT TTCGCTCTGG 20

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF12)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

GTGTGAGGAG GCATTCTTCA 20

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..32
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C19SF)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

GAATCAACTC AAAAAAGTGG AATAGATGTT AC 32

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..32
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C19SR)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

GTAACATCTA TTCCACTTTT TTGAGTTGAT TC 32

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..30
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C20SF)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

ATAGATGTTA CCCTGAGTGA GGAGGCATTC 30

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..30
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C20SR)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

GAATGCCTCC TCACTCAGGG TAACATCTAT 30

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..31
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C21SF)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

CAAGATATTG ACCTCAGTGA AAACAGCGTG C 31

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -

(B) LOCATION: 1..31
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C21SR)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

GCACGCTGTT TTCACTGAGG GCAATATCTT G 31

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..31
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C22SF)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

AAAACAATAA AGGCAAGCAA ACCCAGTGAC C 31

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..31
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C22SR)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

GGTCACTGGG TTTGCTTGCC TTTATTGTTT T 31

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..31
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C23SF)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

TCAGTAAAAA TAAGCAGCTT ATAACTGGCC A 31

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..31
(D) OTHER INFORMATION: /note= "synthetic DNA (primer C23SR)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

TGGCCAGTTA TAAGCTGCTT ATTTTTACTG A 31

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..22
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF14)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

TTGGGGTTTA TTGGAGGAGA TG 22

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DCR1F)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

ACCACCCAGG AACCTTGCCC TGACCACTAC TACACA 36

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DCR1R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

GTCAGGGCAA GGTTCCTGGG TGGTCCACTT AATGGA 36

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DCR2F)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

ACCGTGTGCG CCGAATGCAA GGAAGGGCGC TACCTT 36

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DCR2R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

TTCCTTGCAT TCGGCGCACA CGGTCTTCCA CTTTGC 36

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DCR3F)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

AACCGCGTGT GCAGATGTCC AGATGGGTTC TTCTCA 36

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DCR3R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

ATCTGGACAT CTGCACACGC GGTTGTGGGT GCGATT 36

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DCR4F)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

ACAGTTTGCA AATCCGGAAA CAGTGAATCA ACTCAA 36

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DCR4R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

ACTGTTTCCG GATTTGCAAA CTGTATTTCG CTCTGG 36

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DDD1F)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

AATGTGGAAT AGATATTGAC CTCTGTGAAA ACAGCG 36

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DDD1R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

AGAGGTCAAT ATCTATTCCA CATTTTTGAG TTGATT 36

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DDD2F)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

AGATCATCCA AGACGCACTA AAGCACTCAA AGACGT 36

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..36
(D) OTHER INFORMATION: /note= "synthetic DNA (primer DDD2R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

GCTTTAGTGC GTCTTGGATG ATCTTCTTGA CTATAT 36

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..29
(D) OTHER INFORMATION: /note= "synthetic DNA (primer XhoI F)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

GGCTCGAGCG CCCAGCCGCC GCCTCCAAG 29

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer IF16)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

TTTGAGTGCT TTAGTGCGTG 20

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..30
(D) OTHER INFORMATION: /note= "synthetic DNA (primer CL F)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

TCAGTAAAAA TAAGCTAACT GGAAATGGCC 30

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..30
(D) OTHER INFORMATION: /note= "synthetic DNA (primer CL R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

GGCCATTTCC AGTTAGCTTA TTTTTACTGA 30

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..29
(D) OTHER INFORMATION: /note= "synthetic DNA (primer CC R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

CCGGATCCTC AGTGCTTTAG TGCGTGCAT 29

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..29
(D) OTHER INFORMATION: /note= "synthetic DNA (primer CCD2R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

CCGGATCCTC ATTGGATGAT CTTCTTGAC 29

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..29
(D) OTHER INFORMATION: /note= "synthetic DNA (primer CCD1R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

CCGGATCCTC ATATTCCACA TTTTTGAGT 29

(2) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..29
(D) OTHER INFORMATION: /note= "synthetic DNA (primer CCR4R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

CCGGATCCTC ATTTGCAAAC TGTATTTCG 29

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..29
(D) OTHER INFORMATION: /note= "synthetic DNA (primer CCR3 R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

CCGGATCCTC ATTCGCACAC GCGGTTGTG 29

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 401 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..380
(D) OTHER INFORMATION: /note= "OCIF-C19S"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1               5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
    125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
```

160 165 170

Gln Lys Ser Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
175 180 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
190 195 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
205 210 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220 225 230 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
240 245 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
255 260 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
270 275 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
285 290 295

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300 305 310 315

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
320 325 330

Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
335 340 345

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
350 355 360

Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys
365 370 375

Leu
380

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 401 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..380
(D) OTHER INFORMATION: /note= "OCIF-C20S"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile

-20 -15 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5 1 5 10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
15 20 25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60 65 70 75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
80 85 90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
95 100 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
110 115 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
125 130 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140 145 150 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
160 165 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Ser Glu Glu Ala Phe Phe Arg
175 180 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
190 195 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
205 210 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220 225 230 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
240 245 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
255 260 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
270 275 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
285 290 295

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300 305 310 315

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
320 325 330

Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
335 340 345

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
350 355 360

Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys
365 370 375

Leu
380

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 401 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..380
(D) OTHER INFORMATION: /note= "OCIF-C21S"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20 -15 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5 1 5 10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
15 20 25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60 65 70 75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
80 85 90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
95 100 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
110 115 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
125 130 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140 145 150 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
160 165 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
175 180 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
190 195 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
205 210 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220 225 230 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
240 245 250

Asp Ile Asp Leu Ser Glu Asn Ser Val Gln Arg His Ile Gly His Ala
255 260 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
270 275 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
285 290 295

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300 305 310 315

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
320 325 330

Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
335 340 345

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
350 355 360

Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys
365 370 375

Leu
380

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 401 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..380
(D) OTHER INFORMATION: /note= "OCIF-C22S"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20 -15 -10

Lys Trp Thr Th Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5 1 5 10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
15 20 25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60 65 70 75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
80 85 90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
95 100 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
110 115 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
125 130 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140 145 150 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
160 165 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
175 180 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
190 195 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
205 210 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220 225 230 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
240 245 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
255 260 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
270 275 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Ser Lys
285 290 295

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300 305 310 315

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
320 325 330

Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
335 340 345

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
350 355 360

```
Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys
365                 370                 375

Leu
380
```

(2) INFORMATION FOR SEQ ID NO:66:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 401 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..380
(D) OTHER INFORMATION: /note= "OCIF-C23S"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
                160                 165                 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
            175                 180                 185
```

```
Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
        190                 195                 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
    205                 210                 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220                 225                 230                 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
                240                 245                 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
            255                 260                 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
        270                 275                 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
    285                 290                 295

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300                 305                 310                 315

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
                320                 325                 330

Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
            335                 340                 345

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
        350                 355                 360

Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Ser
    365                 370                 375

Leu
380
```

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 360 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..339
(D) OTHER INFORMATION: /note= "OCIF-DCR1"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Pro Cys Pro Asp His Tyr Tyr Thr Asp Ser
-5                  1                   5                   10
```

```
Trp His Thr Ser Asp Glu Cys Leu Tyr Cys Ser Pro Val Cys Lys Glu
                15                  20                  25

Leu Gln Tyr Val Lys Gln Glu Cys Asn Arg Thr His Asn Arg Val Cys
        30                  35                  40

Glu Cys Lys Glu Gly Arg Tyr Leu Glu Ile Glu Phe Cys Leu Lys His
    45                  50                  55

Arg Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala Gly Thr Pro Glu
60                  65                  70                  75

Arg Asn Thr Val Cys Lys Arg Cys Pro Asp Gly Phe Phe Ser Asn Glu
                80                  85                  90

Thr Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn Cys Ser Val Phe
            95                  100                 105

Gly Leu Leu Leu Thr Gln Lys Gly Asn Ala Thr His Asp Asn Ile Cys
        110                 115                 120

Ser Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile Asp Val Thr Leu
    125                 130                 135

Cys Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr Lys Phe Thr Pro
140                 145                 150                 155

Asn Trp Leu Ser Val Leu Val Asp Asn Leu Pro Gly Thr Lys Val Asn
                160                 165                 170

Ala Glu Ser Val Glu Arg Ile Lys Arg Gln His Ser Ser Gln Glu Gln
            175                 180                 185

Thr Phe Gln Leu Leu Lys Leu Trp Lys His Gln Asn Lys Asp Gln Asp
        190                 195                 200

Ile Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys Glu Asn Ser Val
    205                 210                 215

Gln Arg His Ile Gly His Ala Asn Leu Thr Phe Glu Gln Leu Arg Ser
220                 225                 230                 235

Leu Met Glu Ser Leu Pro Gly Lys Lys Val Gly Ala Glu Asp Ile Glu
                240                 245                 250

Lys Thr Ile Lys Ala Cys Lys Pro Ser Asp Gln Ile Leu Lys Leu Leu
            255                 260                 265

Ser Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu Lys Gly Leu
        270                 275                 280

Met His Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro Lys Thr Val
    285                 290                 295

Thr Gln Ser Leu Lys Lys Thr Ile Arg Phe Leu His Ser Phe Thr Met
300                 305                 310                 315

Tyr Lys Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Gly Asn Gln Val
                320                 325                 330

Gln Ser Val Lys Ile Ser Cys Leu
            335
```

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 359 amino acids

(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..338
(D) OTHER INFORMATION: /note= "OCIF-DCR2"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Glu
        30                  35                  40

Cys Lys Glu Gly Arg Tyr Leu Glu Ile Glu Phe Cys Leu Lys His Arg
    45                  50                  55

Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala Gly Thr Pro Glu Arg
60                  65                  70                  75

Asn Thr Val Cys Lys Arg Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr
                80                  85                  90

Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn Cys Ser Val Phe Gly
            95                  100                 105

Leu Leu Leu Thr Gln Lys Gly Asn Ala Thr His Asp Asn Ile Cys Ser
        110                 115                 120

Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile Asp Val Thr Leu Cys
    125                 130                 135

Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr Lys Phe Thr Pro Asn
140                 145                 150                 155

Trp Leu Ser Val Leu Val Asp Asn Leu Pro Gly Thr Lys Val Asn Ala
                160                 165                 170

Glu Ser Val Glu Arg Ile Lys Arg Gln His Ser Ser Gln Glu Gln Thr
            175                 180                 185

Phe Gln Leu Leu Lys Leu Trp Lys His Gln Asn Lys Asp Gln Asp Ile
        190                 195                 200

Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys Glu Asn Ser Val Gln
    205                 210                 215

Arg His Ile Gly His Ala Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu
220                 225                 230                 235

Met Glu Ser Leu Pro Gly Lys Lys Val Gly Ala Glu Asp Ile Glu Lys
```

```
                    40                  245                 250

Thr Ile Lys Ala Cys Lys Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser
            255                 260                 265

Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu Lys Gly Leu Met
        270                 275                 280

His Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro Lys Thr Val Thr
    285                 290                 295

Gln Ser Leu Lys Lys Thr Ile Arg Phe Leu His Ser Phe Thr Met Tyr
300                 305                 310                 315

Lys Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Gly Asn Gln Val Gln
                320                 325                 330

Ser Val Lys Ile Ser Cys Leu
            335
```

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 363 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..342
(D) OTHER INFORMATION: /note= "OCIF-DCR3"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Arg Cys Pro Asp Gly Phe Phe
                80                  85                  90

Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn Cys
            95                  100                 105

Ser Val Phe Gly Leu Leu Leu Thr Gln Lys Gly Asn Ala Thr His Asp
```

```
        110                 115                 )

Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile Asp
    125                 130                 135

Val Thr Leu Cys Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr Lys
140                 145                 150                 155

Phe Thr Pro Asn Trp Leu Ser Val Leu Val Asp Asn Leu Pro Gly Thr
                160                 165                 170

Lys Val Asn Ala Glu Ser Val Glu Arg Ile Lys Arg Gln His Ser Ser
            175                 180                 185

Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu Trp Lys His Gln Asn Lys
        190                 195                 200

Asp Gln Asp Ile Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys Glu
    205                 210                 215

Asn Ser Val Gln Arg His Ile Gly His Ala Asn Leu Thr Phe Glu Gln
220                 225                 230                 235

Leu Arg Ser Leu Met Glu Ser Leu Pro Gly Lys Lys Val Gly Ala Glu
                240                 245                 250

Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys Pro Ser Asp Gln Ile Leu
            255                 260                 265

Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu
        270                 275                 280

Lys Gly Leu Met His Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro
    285                 290                 295

Lys Thr Val Thr Gln Ser Leu Lys Lys Thr Ile Arg Phe Leu His Ser
300                 305                 310                 315

Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Gly
                320                 325                 330

Asn Gln Val Gln Ser Val Lys Ile Ser Cys Leu
            335                 340
```

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 359 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..338
(D) OTHER INFORMATION: /note= "OCIF-DCR4"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
```

```
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                  10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Ser
        110                 115                 120

Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile Asp Val Thr Leu Cys
    125                 130                 135

Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr Lys Phe Thr Pro Asn
140                 145                 150                 155

Trp Leu Ser Val Leu Val Asp Asn Leu Pro Gly Thr Lys Val Asn Ala
                160                 165                 170

Glu Ser Val Glu Arg Ile Lys Arg Gln His Ser Ser Gln Glu Gln Thr
            175                 180                 185

Phe Gln Leu Leu Lys Leu Trp Lys His Gln Asn Lys Asp Gln Asp Ile
        190                 195                 200

Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys Glu Asn Ser Val Gln
    205                 210                 215

Arg His Ile Gly His Ala Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu
220                 225                 230                 235

Met Glu Ser Leu Pro Gly Lys Lys Val Gly Ala Glu Asp Ile Glu Lys
                240                 245                 250

Thr Ile Lys Ala Cys Lys Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser
            255                 260                 265

Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu Lys Gly Leu Met
        270                 275                 280

His Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro Lys Thr Val Thr
    285                 290                 295

Gln Ser Leu Lys Lys Thr Ile Arg Phe Leu His Ser Phe Thr Met Tyr
300                 305                 310                 315

Lys Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Gly Asn Gln Val Gln
                320                 325                 330

Ser Val Lys Ile Ser Cys Leu
            335
```

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 326 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..305
(D) OTHER INFORMATION: /note= "OCIF-DDD1"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
    125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
                160                 165                 170

Gln Lys Cys Gly Ile Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg
            175                 180                 185

His Ile Gly His Ala Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met
        190                 195                 200

Glu Ser Leu Pro Gly Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr
    205                 210                 215
```

```
Ile Lys Ala Cys Lys Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu
220                 225                 230                 235

Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His
                240                 245                 250

Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln
            255                 260                 265

Ser Leu Lys Lys Thr Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys
        270                 275                 280

Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser
    285                 290                 295

Val Lys Ile Ser Cys Leu
300                 305
```

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 327 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..306
(D) OTHER INFORMATION: /note= "OCIF-DDD2"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                  10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120
```

```
Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
    125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
                160                 165                 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
            175                 180                 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
        190                 195                 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
    205                 210                 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220                 225                 230                 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
                240                 245                 250

Asp Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro Lys Thr Val Thr
            255                 260                 265

Gln Ser Leu Lys Lys Thr Ile Arg Phe Leu His Ser Phe Thr Met Tyr
        270                 275                 280

Lys Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Gly Asn Gln Val Gln
    285                 290                 295

Ser Val Lys Ile Ser Cys Leu
300                 305
```

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 399 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..378
(D) OTHER INFORMATION: /note= "OCIF-CL"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25
```

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60 65 70 75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
80 85 90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
95 100 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
110 115 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
125 130 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140 145 150 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
160 165 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
175 180 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
190 195 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
205 210 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220 225 230 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
240 245 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
255 260 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
270 275 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
285 290 295

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300 305 310 315

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
320 325 330

Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
335 340 345

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
350 355 360

Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser
365 370 375

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 351 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..330
(D) OTHER INFORMATION: /note= "OCIF-CC"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                  10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
    125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
                160                 165                 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
            175                 180                 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
        190                 195                 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
    205                 210                 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220                 225                 230                 235
```

```
Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
                240                 245                 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
            255                 260                 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
        270                 275                 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
    285                 290                 295

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300                 305                 310                 315

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His
                320                 325                 330
```

(2) INFORMATION FOR SEQ ID NO:75:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 272 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..251
(D) OTHER INFORMATION: /note= "OCIF-CDD2"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120
```

```
Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
    125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
                160                 165                 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
            175                 180                 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
        190                 195                 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
    205                 210                 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220                 225                 230                 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
                240                 245                 250
```

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 197 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..176
(D) OTHER INFORMATION: /note= "OCIF-CDD1"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
```

```
                    `0                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
    125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
                160                 165                 170

Gln Lys Cys Gly Ile
            175
```

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 143 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..122
(D) OTHER INFORMATION: /note= "OCIF-CCR4"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                   10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys
```

110 115

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 106 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..85
(D) OTHER INFORMATION: /note= "OCIF-CCR3"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20 -15 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5 1 5 10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
15 20 25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60 65 70 75

Cys Asn Arg Thr His Asn Arg Val Cys Glu
80 85

(2) INFORMATION FOR SEQ ID NO:79:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 393 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..372
(D) OTHER INFORMATION: /note= "OCIF-CBst"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
    -20                 -15                 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5                  1                   5                  10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
            15                  20                  25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
        30                  35                  40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
    45                  50                  55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60                  65                  70                  75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
                80                  85                  90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
            95                  100                 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
        110                 115                 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
    125                 130                 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140                 145                 150                 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
                160                 165                 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
            175                 180                 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
        190                 195                 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
    205                 210                 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220                 225                 230                 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
                240                 245                 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
            255                 260                 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
        270                 275                 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
    285                 290                 295

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300                 305                 310                 315

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
                320                 325                 330

Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
```

33 340 345

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
350 355 360

Phe Leu Glu Met Ile Gly Asn Leu Val
365 370

(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 321 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..300
(D) OTHER INFORMATION: /note= "OCIF-CSph"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20 -15 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5 1 5 10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
15 20 25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60 65 70 75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
80 85 90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
95 100 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
110 115 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
125 130 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140 145 150 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
160 165 170

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg

175 180 185

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
190 195 200

Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile
205 210 215

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
220 225 230 235

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
240 245 250

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
255 260 265

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
270 275 280

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Ser Leu
285 290 295

Asp
300

(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 187 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..166
(D) OTHER INFORMATION: /note= "OCIF-CBsp"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20 -15 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5 1 5 10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
15 20 25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
60 65 70 75

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr

80 85 90

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
95 100 105

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
110 115 120

Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
125 130 135

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
140 145 150 155

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly
160 165

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 84 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: -21..0

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION: 1..63
(D) OTHER INFORMATION: /note= "OCIF-CPst"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
-20 -15 -10

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
-5 1 5 10

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
15 20 25

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
30 35 40

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
45 50 55

Leu Tyr Leu Val
60

(2) INFORMATION FOR SEQ ID NO:83:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1206 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1206
(D) OTHER INFORMATION: /note= "(OCIF-C19S)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AAAGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCTG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCATGCAAA 960

CCCAGTGACC AGATCCTGAA GCTGCTCAGT TTGTGGCGAA TAAAAAATGG CGACCAAGAC 1020

ACCTTGAAGG GCCTAATGCA CGCACTAAAG CACTCAAAGA CGTACCACTT TCCCAAAACT 1080

GTCACTCAGA GTCTAAAGAA GACCATCAGG TTCCTTCACA GCTTCACAAT GTACAAATTG 1140

TATCAGAAGT TATTTTTAGA AATGATAGGT AACCAGGTCC AATCAGTAAA AATAAGCTGC 1200

TTATAA 1206

(2) INFORMATION FOR SEQ ID NO:84:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1206 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1206
(D) OTHER INFORMATION: /note= "(OCIF-C20S)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGAGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCTG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCATGCAAA 960

CCCAGTGACC AGATCCTGAA GCTGCTCAGT TTGTGGCGAA TAAAAAATGG CGACCAAGAC 1020

ACCTTGAAGG GCCTAATGCA CGCACTAAAG CACTCAAAGA CGTACCACTT TCCCAAAACT 1080

GTCACTCAGA GTCTAAAGAA GACCATCAGG TTCCTTCACA GCTTCACAAT GTACAAATTG 1140

TATCAGAAGT TATTTTTAGA AATGATAGGT AACCAGGTCC AATCAGTAAA AATAAGCTGC 1200

TTATAA 1206

(2) INFORMATION FOR SEQ ID NO:85:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1206 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1206
(D) OTHER INFORMATION: /note= "(OCIF-C21S)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCAG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCATGCAAA 960

CCCAGTGACC AGATCCTGAA GCTGCTCAGT TTGTGGCGAA TAAAAAATGG CGACCAAGAC 1020

ACCTTGAAGG GCCTAATGCA CGCACTAAAG CACTCAAAGA CGTACCACTT TCCCAAAACT 1080

GTCACTCAGA GTCTAAAGAA GACCATCAGG TTCCTTCACA GCTTCACAAT GTACAAATTG 1140

TATCAGAAGT TATTTTTAGA AATGATAGGT AACCAGGTCC AATCAGTAAA AATAAGCTGC 1200

TTATAA 1206

(2) INFORMATION FOR SEQ ID NO:86:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1206 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1206
(D) OTHER INFORMATION: /note= "(OCIF-C22S)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCTG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCAAGCAAA 960

CCCAGTGACC AGATCCTGAA GCTGCTCAGT TTGTGGCGAA TAAAAAATGG CGACCAAGAC 1020

ACCTTGAAGG GCCTAATGCA CGCACTAAAG CACTCAAAGA CGTACCACTT TCCCAAAACT 1080

GTCACTCAGA GTCTAAAGAA GACCATCAGG TTCCTTCACA GCTTCACAAT GTACAAATTG 1140

TATCAGAAGT TATTTTTAGA AATGATAGGT AACCAGGTCC AATCAGTAAA AATAAGCTGC 1200

TTATAA 1206

(2) INFORMATION FOR SEQ ID NO:87:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1206 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1206
(D) OTHER INFORMATION: /note= "(OCIF-C23S)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCTG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCATGCAAA 960

CCCAGTGACC AGATCCTGAA GCTGCTCAGT TTGTGGCGAA TAAAAAATGG CGACCAAGAC 1020

ACCTTGAAGG GCCTAATGCA CGCACTAAAG CACTCAAAGA CGTACCACTT TCCCAAAACT 1080

GTCACTCAGA GTCTAAAGAA GACCATCAGG TTCCTTCACA GCTTCACAAT GTACAAATTG 1140

TATCAGAAGT TATTTTTAGA AATGATAGGT AACCAGGTCC AATCAGTAAA AATAAGCAGC 1200

TTATAA 1206

(2) INFORMATION FOR SEQ ID NO:88:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1083 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1083
(D) OTHER INFORMATION: /note= "(OCIF-DCR1)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAACCTT GCCCTGACCA CTACTACACA GACAGCTGGC ACACCAGTGA CGAGTGTCTA 120

TACTGCAGCC CCGTGTGCAA GGAGCTGCAG TACGTCAAGC AGGAGTGCAA TCGCACCCAC 180

AACCGCGTGT GCGAATGCAA GGAAGGGCGC TACCTTGAGA TAGAGTTCTG CTTGAAACAT 240

AGGAGCTGCC CTCCTGGATT TGGAGTGGTG CAAGCTGGAA CCCCAGAGCG AAATACAGTT 300

TGCAAAAGAT GTCCAGATGG GTTCTTCTCA AATGAGACGT CATCTAAAGC ACCCTGTAGA 360

AAACACACAA ATTGCAGTGT CTTTGGTCTC CTGCTAACTC AGAAAGGAAA TGCAACACAC 420

GACAACATAT GTTCCGGAAA CAGTGAATCA ACTCAAAAAT GTGGAATAGA TGTTACCCTG 480

TGTGAGGAGG CATTCTTCAG GTTTGCTGTT CCTACAAAGT TTACGCCTAA CTGGCTTAGT 540

GTCTTGGTAG ACAATTTGCC TGGCACCAAA GTAAACGCAG AGAGTGTAGA GAGGATAAAA 600

CGGCAACACA GCTCACAAGA ACAGACTTTC CAGCTGCTGA AGTTATGGAA ACATCAAAAC 660

AAAGACCAAG ATATAGTCAA GAAGATCATC CAAGATATTG ACCTCTGTGA AAACAGCGTG 720

CAGCGGCACA TTGGACATGC TAACCTCACC TTCGAGCAGC TTCGTAGCTT GATGGAAAGC 780

TTACCGGGAA AGAAAGTGCC AGCAGAAGAC ATTGAAAAAA CAATAAAGCC ATGCAAACCC 840

AGTGACCAGA TCCTGAAGCT GCTCAGTTTG TGGCGAATAA AAAATGGCGA CCAAGACACC 900

TTGAAGGGCC TAATGCACGC ACTAAAGCAC TCAAAGACGT ACCACTTTCC CAAAACTGTC 960

ACTCAGAGTC TAAAGAAGAC CATCAGGTTC CTTCACAGCT TCACAATGTA CAAATTGTAT 1020

CAGAAGTTAT TTTTAGAAAT GATAGGTAAC CAGGTCCAAT CAGTAAAAAT AAGCTGCTTA 1080

TAA 1083

(2) INFORMATION FOR SEQ ID NO:89:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1080 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1080
(D) OTHER INFORMATION: /note= "(OCIF-DCR2)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCG AATGCAAGGA AGGGCGCTAC CTTGAGATAG AGTTCTGCTT GAAACATAGG 240

AGCTGCCCTC CTGGATTTGG AGTGGTGCAA GCTGGAACCC CAGAGCGAAA TACAGTTTGC 300

AAAAGATGTC CAGATGGGTT CTTCTCAAAT GAGACGTCAT CTAAAGCACC CTGTAGAAAA 360

CACACAAATT GCAGTGTCTT TGGTCTCCTG CTAACTCAGA AAGGAAATGC AACACACGAC 420

AACATATGTT CCGGAAACAG TGAATCAACT CAAAAATGTG GAATAGATGT TACCCTGTGT 480

GAGGAGGCAT TCTTCAGGTT TGCTGTTCCT ACAAAGTTTA CGCCTAACTG GCTTAGTGTC 540

TTGGTAGACA ATTTGCCTGG CACCAAAGTA AACGCAGAGA GTGTAGAGAG GATAAAACGG 600

CAACACAGCT CACAAGAACA GACTTTCCAG CTGCTGAAGT TATGGAAACA TCAAAACAAA 660

GACCAAGATA TAGTCAAGAA GATCATCCAA GATATTGACC TCTGTGAAAA CAGCGTGCAG 720

CGGCACATTG GACATGCTAA CCTCACCTTC GAGCAGCTTC GTAGCTTGAT GGAAAGCTTA 780

CCGGGAAAGA AAGTGGGAGC AGAAGACATT GAAAAAACAA TAAAGGCATG CAAACCCAGT 840

GACCAGATCC TGAAGCTGCT CAGTTTGTGG CGAATAAAAA ATGGCGACCA AGACACCTTG 900

AAGGGCCTAA TGCACGCACT AAAGCACTCA AAGACGTACC ACTTTCCCAA AACTGTCACT 960

CAGAGTCTAA AGAAGACCAT CAGGTTCCTT CACAGCTTCA CAATGTACAA ATTGTATCAG 1020

AAGTTATTTT TAGAAATGAT AGGTAACCAG GTCCAATCAG TAAAAATAAG CTGCTTATAA 1080

(2) INFORMATION FOR SEQ ID NO:90:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1092 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1092
(D) OTHER INFORMATION: /note= "(OCIF-DCR3)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCAGATG TCCAGATGGG TTCTTCTCAA ATGAGACGTC ATCTAAAGCA 360

CCCTGTAGAA AACACACAAA TTGCAGTGTC TTTGGTCTCC TGCTAACTCA GAAAGGAAAT 420

GCAACACACG ACAACATATG TTCCGGAAAC AGTGAATCAA CTCAAAAATG TGGAATAGAT 480

GTTACCCTGT GTGAGGAGGC ATTCTTCAGG TTTGCTGTTC CTACAAAGTT TACGCCTAAC 540

TGGCTTAGTG TCTTGGTAGA CAATTTGCCT GGCACCAAAG TAAACGCAGA GAGTGTAGAG 600

AGGATAAAAC GGCAACACAG CTCACAAGAA CAGACTTTCC AGCTGCTGAA GTTATGGAAA 660

CATCAAAACA AAGACCAAGA TATAGTCAAG AAGATCATCC AAGATATTGA CCTCTGTGAA 720

AACAGCGTGC AGCGGCACAT TGGACATGCT AACCTCACCT TCGAGCAGCT TCGTAGCTTG 780

ATGGAAAGCT TACCGGGAAA GAAAGTGGGA GCAGAAGACA TTGAAAAAAC AATAAAGGCA 840

TGCAAACCCA GTGACCAGAT CCTGAAGCTG CTCAGTTTGT GGCGAATAAA AAATGGCGAC 900

CAAGACACCT TGAAGGGCCT AATGCACGCA CTAAAGCACT CAAAGACGTA CCACTTTCCC 960

AAAACTGTCA CTCAGAGTCT AAAGAAGACC ATCAGGTTCC TTCACAGCTT CACAATGTAC 1020

AAATTGTATC AGAAGTTATT TTTAGAAATG ATAGGTAACC AGGTCCAATC AGTAAAAATA 1080

AGCTGCTTAT AA 1092

(2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1080 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1080
(D) OTHER INFORMATION: /note= "(OCIF-DCR4)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAT CCGGAAACAG TGAATCAACT CAAAAATGTG GAATAGATGT TACCCTGTGT 480

GAGGAGGCAT TCTTCAGGTT TGCTGTTCCT ACAAAGTTTA CGCCTAACTG GCTTAGTGTC 540

TTGGTAGACA ATTTGCCTGG CACCAAAGTA AACGCAGAGA GTGTAGAGAG GATAAAACGG 600

CAACACAGCT CACAAGAACA GACTTTCCAG CTGCTGAAGT TATGGAAACA TCAAAACAAA 660

GACCAAGATA TAGTCAAGAA GATCATCCAA GATATTGACC TCTGTGAAAA CAGCGTGCAG 720

CGGCACATTG GACATGCTAA CCTCACCTTC GAGCAGCTTC GTAGCTTGAT GGAAAGCTTA 780

CCGGGAAAGA AAGTGGGAGC AGAAGACATT GAAAAAACAA TAAAGGCATG CAAACCCAGT 840

GACCAGATCC TGAAGCTGCT CAGTTTGTGG CGAATAAAAA ATGGCGACCA AGACACCTTG 900

AAGGGCCTAA TGCACGCACT AAAGCACTCA AAGACGTACC ACTTTCCCAA AACTGTCACT 960

CAGAGTCTAA AGAAGACCAT CAGGTTCCTT CACAGCTTCA CAATGTACAA ATTGTATCAG 1020

AAGTTATTTT TAGAAATGAT AGGTAACCAG GTCCAATCAG TAAAAATAAG CTGCTTATAA 1080

(2) INFORMATION FOR SEQ ID NO:92:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 981 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..981
(D) OTHER INFORMATION: /note= "(OCIF-DDD1)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATATTGAC 600

CTCTGTGAAA ACAGCGTGCA GCGGCACATT GGACATGCTA ACCTCACCTT CGAGCAGCTT 660

CGTAGCTTGA TGGAAAGCTT ACCGGGAAAG AAAGTGGGAG CAGAAGACAT TGAAAAAACA 720

ATAAAGGCAT GCAAACCCAG TGACCAGATC CTGAAGCTGC TCAGTTTGTG GCGAATAAAA 780

AATGGCGACC AAGACACCTT GAAGGGCCTA ATGCACGCAC TAAAGCACTC AAAGACGTAC 840

CACTTTCCCA AAACTGTCAC TCAGAGTCTA AAGAAGACCA TCAGGTTCCT TCACAGCTTC 900

ACAATGTACA AATTGTATCA GAAGTTATTT TTAGAAATGA TAGGTAACCA GGTCCAATCA 960

GTAAAAATAA GCTGCTTATA A 981

(2) INFORMATION FOR SEQ ID NO:93:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 984 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..984
(D) OTHER INFORMATION: /note= "(OCIF-DDD2)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGACG CACTAAAGCA CTCAAAGACG 840

TACCACTTTC CCAAAACTGT CACTCAGAGT CTAAAGAAGA CCATCAGGTT CCTTCACAGC 900

TTCACAATGT ACAAATTGTA TCAGAAGTTA TTTTTAGAAA TGATAGGTAA CCAGGTCCAA 960

TCAGTAAAAA TAAGCTGCTT ATAA 984

(2) INFORMATION FOR SEQ ID NO:94:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1200 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1200
(D) OTHER INFORMATION: /note= "(OCIF-CL)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCTG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCATGCAAA 960

CCCAGTGACC AGATCCTGAA GCTGCTCAGT TTGTGGCGAA TAAAAAATGG CGACCAAGAC 1020

ACCTTGAAGG GCCTAATGCA CGCACTAAAG CACTCAAAGA CGTACCACTT TCCCAAAACT 1080

GTCACTCAGA GTCTAAAGAA GACCATCAGG TTCCTTCACA GCTTCACAAT GTACAAATTG 1140

TATCAGAAGT TATTTTTAGA AATGATAGGT AACCAGGTCC AATCAGTAAA AATAAGCTAA 1200

(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1056 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1056
(D) OTHER INFORMATION: /note= "(OCIF-CC)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCTG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCATGCAAA 960

CCCAGTGACC AGATCCTGAA GCTGCTCAGT TTGTGGCGAA TAAAAAATGG CGACCAAGAC 1020

ACCTTGAAGG GCCTAATGCA CGCACTAAAG CACTGA 1056

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 819 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..819
(D) OTHER INFORMATION: /note= "(OCIF-CDD2)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

```
ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC    60
CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG   120
TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC   180
GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT   240
CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC   300
CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA   360
CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA   420
GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT   480
AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA   540
CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC   600
CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT   660
AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA   720
AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA   780
AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAATGA                          819
```

(2) INFORMATION FOR SEQ ID NO:97:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 594 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..594
(D) OTHER INFORMATION: /note= "(OCIF-CDD1)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

```
ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC    60
CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG   120
TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC   180
GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT   240
```

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT ATGA 594

(2) INFORMATION FOR SEQ ID NO:98:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 432 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..432
(D) OTHER INFORMATION: /note= "(OCIF-CCR4)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAT GA 432

(2) INFORMATION FOR SEQ ID NO:99:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 321 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..321
(D) OTHER INFORMATION: /note= "(OCIF-CCR3)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG A 321

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1182 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1182
(D) OTHER INFORMATION: /note= "(OCIF-CBst)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCTG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCATGCAAA 960

CCCAGTGACC AGATCCTGAA GCTGCTCAGT TTGTGGCGAA TAAAAAATGG CGACCAAGAC 1020

ACCTTGAAGG GCCTAATGCA CGCACTAAAG CACTCAAAGA CGTACCACTT TCCCAAAACT 1080

GTCACTCAGA GTCTAAAGAA GACCATCAGG TTCCTTCACA GCTTCACAAT GTACAAATTG 1140

TATCAGAAGT TATTTTTAGA AATGATAGGT AACCTAGTCT AG 1182

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 966 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..966
(D) OTHER INFORMATION: /note= "(OCIF-CSph)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG AAACAGTGAA TCAACTCAAA AATGTGGAAT AGATGTTACC 600

CTGTGTGAGG AGGCATTCTT CAGGTTTGCT GTTCCTACAA AGTTTACGCC TAACTGGCTT 660

AGTGTCTTGG TAGACAATTT GCCTGGCACC AAAGTAAACG CAGAGAGTGT AGAGAGGATA 720

AAACGGCAAC ACAGCTCACA AGAACAGACT TTCCAGCTGC TGAAGTTATG GAAACATCAA 780

AACAAAGACC AAGATATAGT CAAGAAGATC ATCCAAGATA TTGACCTCTG TGAAAACAGC 840

GTGCAGCGGC ACATTGGACA TGCTAACCTC ACCTTCGAGC AGCTTCGTAG CTTGATGGAA 900

AGCTTACCGG GAAAGAAAGT GGGAGCAGAA GACATTGAAA AAACAATAAA GGCTAGTCTA 960

GACTAG 966

(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 564 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..564

(D) OTHER INFORMATION: /note= "(OCIF-CBsp)'

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACTGCA GCCCCGTGTG CAAGGAGCTG CAGTACGTCA AGCAGGAGTG CAATCGCACC 300

CACAACCGCG TGTGCGAATG CAAGGAAGGG CGCTACCTTG AGATAGAGTT CTGCTTGAAA 360

CATAGGAGCT GCCCTCCTGG ATTTGGAGTG GTGCAAGCTG GAACCCCAGA GCGAAATACA 420

GTTTGCAAAA GATGTCCAGA TGGGTTCTTC TCAAATGAGA CGTCATCTAA AGCACCCTGT 480

AGAAAACACA CAAATTGCAG TGTCTTTGGT CTCCTGCTAA CTCAGAAAGG AAATGCAACA 540

CACGACAACA TATGTTCCGG CTAG 564

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 255 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..255
(D) OTHER INFORMATION: /note= "(OCIF-Pst)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

ATGAACAACT TGCTGTGCTG CGCGCTCGTG TTTCTGGACA TCTCCATTAA GTGGACCACC 60

CAGGAAACGT TTCCTCCAAA GTACCTTCAT TATGACGAAG AAACCTCTCA TCAGCTGTTG 120

TGTGACAAAT GTCCTCCTGG TACCTACCTA AAACAACACT GTACAGCAAA GTGGAAGACC 180

GTGTGCGCCC CTTGCCCTGA CCACTACTAC ACAGACAGCT GGCACACCAG TGACGAGTGT 240

CTATACCTAG TCTAG 255

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1317 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..1317

(D) OTHER INFORMATION: /note= "human OCIF genomic DNA-1"

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: 1173..1202
(D) OTHER INFORMATION: /note= "amino acid residues -21 to -12"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

CTGGAGACAT ATAACTTGAA CACTTGGCCC TGATGGGGAA GCAGCTCTGC AGGGACTTTT 60

TCAGCCATCT GTAAACAATT TCAGTGGCAA CCCGCGAACT GTAATCCATG AATGGGACCA 120

CACTTTACAA GTCATCAAGT CTAACTTCTA GACCAGGGAA TTAATGGGGG AGACAGCGAA 180

CCCTAGAGCA AAGTGCCAAA CTTCTGTCGA TAGCTTGAGG CTAGTGGAAA GACCTCGAGG 240

AGGCTACTCC AGAAGTTCAG CGCGTAGGAA GCTCCGATAC CAATAGCCCT TTGATGATGG 300

TGGGGTTGGT GAAGGGAACA GTGCTCCGCA AGGTTATCCC TGCCCCAGGC AGTCCAATTT 360

TCACTCTGCA GATTCTCTCT GGCTCTAACT ACCCCAGATA ACAAGGAGTG AATGCAGAAT 420

AGCACGGGCT TTAGGGCCAA TCAGACATTA GTTAGAAAAA TTCCTACTAC ATGGTTTATG 480

TAAACTTGAA GATGAATGAT TGCGAACTCC CCGAAAAGGG CTCAGACAAT GCCATGCATA 540

AAGAGGGGCC CTGTAATTTG AGGTTTCAGA ACCCGAAGTG AAGGGGTCAG GCAGCCGGGT 600

ACGGCGGAAA CTCACAGCTT TCGCCCAGCG AGAGGACAAA GGTCTGGGAC ACACTCCAAC 660

TGCGTCCGGA TCTTGGCTGG ATCGGACTCT CAGGGTGGAG GAGACACAAG CACAGCAGCT 720

GCCCAGCGTG TGCCCAGCCC TCCCACCGCT GGTCCCGGCT GCCAGGAGGC TGGCCGCTGG 780

CGGGAAGGGG CCGGGAAACC TCAGAGCCCC GCGGAGACAG CAGCCGCCTT GTTCCTCAGC 840

CCGGTGGCTT TTTTTTCCCC TGCTCTCCCA GGGGACAGAC ACCACCGCCC CACCCCTCAC 900

GCCCCACCTC CCTGGGGGAT CCTTTCCGCC CCAGCCCTGA AAGCGTTAAT CCTGGAGCTT 960

TCTGCACACC CCCCGACCGC TCCCGCCCAA GCTTCCTAAA AAAGAAAGGT GCAAAGTTTG 1020

GTCCAGGATA GAAAAATGAC TGATCAAAGG CAGGCGATAC TTCCTGTTGC CGGGACGCTA 1080

TATATAACGT GATGAGCGCA CGGGCTGCGG AGACGCACCG GAGCGCTCGC CCAGCCGCCG 1140

CCTCCAAGCC CCTGAGGTTT CCGGGGACCA CAATGAACAA GTTGCTGTGC TGCGCGCTCG 1200

TGGTAAGTCC CTGGGCCAGC CGACGGGTGC CCGGCGCCTG GGGAGGCTGC TGCCACCTGG 1260

TCTCCCAACC TCCCAGCGGA CCGGCGGGGA AAAAGGCTCC ACTCGCTCCC TCCCAAG 1317

(2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10190 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: sig_peptide
(B) LOCATION: 130..162

(D) OTHER INFORMATION: /note= "amino acid residues -11 to -1"

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: join(130..162, 163..498, 4503..4694, 6715..6939, 8960..9346)

(ix) FEATURE:
(A) NAME/KEY: mat_peptide
(B) LOCATION: join(163..498, 4503..4694, 6715..6939, 8960..9346)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

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GCTTACTTTG TGCCAAATCT CATTAGGCTT AAGGTAATAC AGGACTTTGA GTCAAATGAT      60

ACTGTTGCAC ATAAGAACAA ACCTATTTTC ATGCTAAGAT GATGCCACTG TGTTCCTTTC     120

TCCTTCTAG TTT CTG GAC ATC TCC ATT AAG TGG ACC ACC CAG GAA ACG          168
          Phe Leu Asp Ile Ser Ile Lys Trp Thr Thr Gln Glu Thr
          -11 -10                  -5                   1

TTT CCT CCA AAG TAC CTT CAT TAT GAC GAA GAA ACC TCT CAT CAG CTG        216
Phe Pro Pro Lys Tyr Leu His Tyr Asp Glu Glu Thr Ser His Gln Leu
          5                  10                  15

TTG TGT GAC AAA TGT CCT CCT GGT ACC TAC CTA AAA CAA CAC TGT ACA        264
Leu Cys Asp Lys Cys Pro Pro Gly Thr Tyr Leu Lys Gln His Cys Thr
     20                  25                  30

GCA AAG TGG AAG ACC GTG TGC GCC CCT TGC CCT GAC CAC TAC TAC ACA        312
Ala Lys Trp Lys Thr Val Cys Ala Pro Cys Pro Asp His Tyr Tyr Thr
 35                  40                  45                  50

GAC AGC TGG CAC ACC AGT GAC GAG TGT CTA TAC TGC AGC CCC GTG TGC        360
Asp Ser Trp His Thr Ser Asp Glu Cys Leu Tyr Cys Ser Pro Val Cys
                 55                  60                  65

AAG GAG CTG CAG TAC GTC AAG CAG GAG TGC AAT CGC ACC CAC AAC CGC        408
Lys Glu Leu Gln Tyr Val Lys Gln Glu Cys Asn Arg Thr His Asn Arg
            70                  75                  80

GTG TGC GAA TGC AAG GAA GGG CGC TAC CTT GAG ATA GAG TTC TGC TTG        456
Val Cys Glu Cys Lys Glu Gly Arg Tyr Leu Glu Ile Glu Phe Cys Leu
         85                  90                  95

AAA CAT AGG AGC TGC CCT CCT GGA TTT GGA GTG GTG CAA GCT                 498
Lys His Arg Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala
    100                 105                 110

GGTACGTGTC AATGTGCAGC AAAATTAATT AGGATCATGC AAAGTCAGAT AGTTGTGACA      558

GTTTAGGAGA ACACTTTTGT TCTGATGACA TTATAGGATA GCAAATTGCA AAGGTAATGA      618

AACCTGCCAG GTAGGTACTA TGTGTCTGGA GTGCTTCCAA AGGACCATTG CTCAGAGGAA      678

TACTTTGCCA CTACAGGGCA ATTTAATGAC AAATCTCAAA TGCAGCAAAT TATTCTCTCA      738

TGAGATGCAT GATGGTTTTT TTTTTTTTTT TTAAAGAAAC AAACTCAAGT TGCACTATTG      798

ATAGTTGATC TATACCTCTA TATTTCACTT CAGCATGGAC ACCTTCAAAC TGCAGCACTT      858

TTTGACAAAC ATCAGAAATG TTAATTTATA CCAAGAGAGT AATTATGCTC ATATTAATGA      918

GACTCTGGAG TGCTAACAAT AAGCAGTTAT AATTAATTAT GTAAAAAATG AGAATGGTGA      978

GGGGAATTGC ATTTCATTAT TAAAAACAAG GCTAGTTCTT CCTTTAGCAT GGGAGCTGAG     1038
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TGTTTGGGAG GGTAAGGACT ATAGCAGAAT CTCTTCAATG AGCTTATTCT TTATCTTAGA 1098

CAAAACAGAT TGTCAAGCCA AGAGCAAGCA CTTGCCTATA AACCAAGTGC TTTCTCTTTT 1158

GCATTTTGAA CAGCATTGGT CAGGGCTCAT GTGTATTGAA TCTTTTAAAC CAGTAACCCA 1218

CGTTTTTTTT CTGCCACATT TGCGAAGCTT CAGTGCAGCC TATAACTTTT CATAGCTTGA 1278

GAAAATTAAG AGTATCCACT TACTTAGATG GAAGAAGTAA TCAGTATAGA TTCTGATGAC 1338

TCAGTTTGAA GCAGTGTTTC TCAACTGAAG CCCTGCTGAT ATTTTAAGAA ATATCTGGAT 1398

TCCTAGGCTG GACTCCTTTT TGTGGGCAGC TGTCCTGCGC ATTGTAGAAT TTTGGCAGCA 1458

CCCCTGGACT CTAGCCACTA GATACCAATA GCAGTCCTTC CCCCATGTGA CAGCCAAAAA 1518

TGTCTTCAGA CACTGTCAAA TGTCGCCAGG TGGCAAAATC ACTCCTGGTT GAGAACAGGG 1578

TCATCAATGC TAAGTATCTG TAACTATTTT AACTCTCAAA ACTTGTGATA TACAAAGTCT 1638

AAATTATTAG ACGACCAATA CTTTAGGTTT AAAGGCATAC AAATGAAACA TTCAAAAATC 1698

AAAATCTATT CTGTTTCTCA AATAGTGAAT CTTATAAAAT TAATCACAGA AGATGCAAAT 1758

TGCATCAGAG TCCCTTAAAA TTCCTCTTCG TATGAGTATT TGAGGGAGGA ATTGGTGATA 1818

GTTCCTACTT TCTATTGGAT GGTACTTTGA GACTCAAAAG CTAAGCTAAG TTGTGTGTGT 1878

GTCAGGGTGC GGGGTGTGGA ATCCCATCAG ATAAAAGCAA ATCCATGTAA TTCATTCAGT 1938

AAGTTGTATA TGTAGAAAAA TGAAAAGTGG GCTATGCAGC TTGGAAACTA GAGAATTTTG 1998

AAAAATAATG GAAATCACAA GGATCTTTCT TAAATAAGTA AGAAAATCTG TTTGTAGAAT 2058

GAAGCAAGCA GGCAGCCAGA AGACTCAGAA CAAAAGTACA CATTTTACTC TGTGTACACT 2118

GGCAGCACAG TGGGATTTAT TTACCTCTCC CTCCCTAAAA ACCCACACAG CGGTTCCTCT 2178

TGGGAAATAA GAGGTTTCCA GCCCAAAGAG AAGGAAAGAC TATGTGGTGT TACTCTAAAA 2238

AGTATTTAAT AACCGTTTTG TTGTTGCTGT TGCTGTTTTG AAATCAGATT GTCTCCTCTC 2298

CATATTTTAT TTACTTCATT CTGTTAATTC CTGTGGAATT ACTTAGAGCA AGCATGGTGA 2358

ATTCTCAACT GTAAAGCCAA ATTTCTCCAT CATTATAATT TCACATTTTG CCTGGCAGGT 2418

TATAATTTTT ATATTTCCAC TGATAGTAAT AAGGTAAAAT CATTACTTAG ATGGATAGAT 2478

CTTTTTCATA AAAAGTACCA TCAGTTATAG AGGGAAGTCA TGTTCATGTT CAGGAAGGTC 2538

ATTAGATAAA GCTTCTGAAT ATATTATGAA ACATTAGTTC TGTCATTCTT AGATTCTTTT 2598

TGTTAAATAA CTTTAAAAGC TAACTTACCT AAAAGAAATA TCTGACACAT ATGAACTTCT 2658

CATTAGGATG CAGGAGAAGA CCCAAGCCAC AGATATGTAT CTGAAGAATG AACAAGATTC 2718

TTAGGCCCGG CACGGTGGCT CACATCTGTA ATCTCAAGAG TTTGAGAGGT CAAGGCGGGC 2778

AGATCACCTG AGGTCAGGAG TTCAAGACCA GCCTGGCCAA CATGATGAAA CCCTGCCTCT 2838

ACTAAAAATA CAAAAATTAG CAGGGCATGG TGGTGCATGC CTGCAACCCT AGCTACTCAG 2898

GAGGCTGAGA CAGGAGAATC TCTTGAACCC TCGAGGCGGA GGTTGTGGTG AGCTGAGATC 2958

CCTCTACTGC ACTCCAGCCT GGGTGACAGA GATGAGACTC CGTCCCTGCC GCCGCCCCCG 3018

CCTTCCCCCC CAAAAAGATT CTTCTTCATG CAGAACATAC GGCAGTCAAC AAAGGGAGAC 3078

CTGGGTCCAG GTGTCCAAGT CACTTATTTC GAGTAAATTA GCAATGAAAG AATGCCATGG 3138

AATCCCTGCC CAAATACCTC TGCTTATGAT ATTGTAGAAT TTGATATAGA GTTGTATCCC 3198

ATTTAAGGAG TAGGATGTAG TAGGAAAGTA CTAAAAACAA ACACACAAAC AGAAAACCCT 3258

CTTTGCTTTG TAAGGTGGTT CCTAAGATAA TGTCAGTGCA ATGCTGGAAA TAATATTTAA 3318

TATGTGAAGG TTTTAGGCTG TGTTTTCCCC TCCTGTTCTT TTTTTCTGCC AGCCCTTTGT 3378

CATTTTTGCA GGTCAATGAA TCATGTAGAA AGAGACAGGA GATGAAACTA GAACCAGTCC 3438

ATTTTGCCCC TTTTTTTATT TTCTGGTTTT GGTAAAAGAT ACAATGAGGT AGGAGGTTGA 3498

GATTTATAAA TGAAGTTTAA TAAGTTTCTG TAGCTTTGAT TTTTCTCTTT CATATTTGTT 3558

ATCTTGCATA AGCCAGAATT GGCCTGTAAA ATCTACATAT GGATATTGAA GTCTAAATCT 3618

GTTCAACTAG CTTACACTAG ATGGAGATAT TTTCATATTC AGATACACTG GAATGTATGA 3678

TCTAGCCATG CGTAATATAG TCAAGTGTTT GAAGGTATTT ATTTTTAATA GCGTCTTTAG 3738

TTGTGGACTG GTTCAAGTTT TTCTGCCAAT GATTTCTTCA AATTTATCAA ATATTTTTCC 3798

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TAAACAGTTT AAGCAAATGG TATATCATCT TCCGTTTACT ATGTAGCTTA ACTGCAGGCT 3918

TACGCTTTTG AGTCAGCGGC CAACTTTATT GCCACCTTCA AAAGTTTATT ATAATGTTGT 3978

AAATTTTTAC TTCTCAAGGT TAGCATACTT AGGAGTTGCT TCACAATTAG GATTCAGGAA 4038

AGAAAGAACT TCAGTAGGAA CTGATTGGAA TTTAATGATG CAGCATTCAA TGGGTACTAA 4098

TTTCAAAGAA TGATATTACA GCAGACACAC AGCAGTTATC TTGATTTTCT AGGAATAATT 4158

GTATGAAGAA TATGGCTGAC AACACGGCCT TACTGCCACT CAGCGGAGGC TGGACTAATG 4218

AACACCCTAC CCTTCTTTCC TTTCCTCTCA CATTTCATGA GCGTTTTGTA GGTAACGAGA 4278

AAATTGACTT GCATTTGCAT TACAAGGAGG AGAAACTGGC AAAGGGGATG ATGGTGGAAG 4338

TTTTGTTCTG TCTAATGAAG TGAAAAATGA AAATGCTAGA GTTTTGTGCA ACATAATAGT 4398

AGCAGTAAAA ACCAAGTGAA AAGTCTTTCC AAAACTGTGT TAAGAGGGCA TCTGCTGGGA 4458

AACGATTTGA GGAGAAGGTA CTAAATTGCT TGGTATTTTC CGTA GGA ACC CCA GAG 4514
Gly Thr Pro Glu
115

CGA AAT ACA GTT TGC AAA AGA TGT CCA GAT GGG TTC TTC TCA AAT GAG 4562
Arg Asn Thr Val Cys Lys Arg Cys Pro Asp Gly Phe Phe Ser Asn Glu
120 125 130

ACG TCA TCT AAA GCA CCC TGT AGA AAA CAC ACA AAT TGC AGT GTC TTT 4610
Thr Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn Cys Ser Val Phe
135 140 145

GGT CTC CTG CTA ACT CAG AAA GGA AAT GCA ACA CAC GAC AAC ATA TGT 4658
Gly Leu Leu Leu Thr Gln Lys Gly Asn Ala Thr His Asp Asn Ile Cys
150 155 160

TCC GGA AAC AGT GAA TCA ACT CAA AAA TGT GGA ATA GGTAATTACA 4704
Ser Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile
165 170 175

TTCCAAAATA CGTCTTTGTA CGATTTTGTA GTATCATCTC TCTCTCTGAG TTGAACACAA 4764

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GGCCTCCAGC CACATTCTTG GTCAAACTTA CATTTTCCCT TTCTTGAATC TTAACCAGCT   4824
AAGGCTACTC TCGATGCATT ACTGCTAAAG CTACCACTCA GAATCTCTCA AAAACTCATC   4884
TTCTCACAGA TAACACCTCA AAGCTTGATT TTCTCTCCTT TCACACTGAA ATCAAATCTT   4944
GCCCATAGGC AAAGGGCAGT GTCAAGTTTG CCACTGAGAT GAAATTAGGA GAGTCCAAAC   5004
TGTAGAATTC ACGTTGTGTG TTATTACTTT CACGAATGTC TGTATTATTA ACTAAAGTAT   5064
ATATTGGCAA CTAAGAAGCA AAGTGATATA AACATGATGA CAAATTAGGC CAGGCATGGT   5124
GGCTTACTCC TATAATCCCA ACATTTTGGG GGGCCAAGGT AGGCAGATCA CTTGAGGTCA   5184
GGATTTCAAG ACCAGCCTGA CCAACATGGT GAAACCTTGT CTCTACTAAA AATACAAAAA   5244
TTAGCTGGGC ATGGTAGCAG GCACTTCTAG TACCAGCTAC TCAGGGCTGA GGCAGGAGAA   5304
TCGCTTGAAC CCAGGAGATG GAGGTTGCAG TGAGCTGAGA TTGTACCACT GCACTCCAGT   5364
CTGGGCAACA GAGCAAGATT TCATCACACA CACACACACA CACACACACA CACACATTAG   5424
AAATGTGTAC TTGGCTTTGT TACCTATGGT ATTAGTGCAT CTATTGCATG GAACTTCCAA   5484
GCTACTCTGG TTGTGTTAAG CTCTTCATTG GGTACAGGTC ACTAGTATTA AGTTCAGGTT   5544
ATTCGGATGC ATTCCACGGT AGTGATGACA ATTCATCAGG CTAGTGTGTG TGTTCACCTT   5604
GTCACTCCCA CCACTAGACT AATCTCAGAC CTTCACTCAA AGACACATTA CACTAAAGAT   5664
GATTTGCTTT TTTGTGTTTA ATCAAGCAAT GGTATAAACC AGCTTGACTC TCCCCAAACA   5724
GTTTTTCGTA CTACAAAGAA GTTTATGAAG CAGAGAAATG TGAATTGATA TATATATGAG   5784
ATTCTAACCC AGTTCCAGCA TTGTTTCATT GTGTAATTGA AATCATAGAC AAGCCATTTT   5844
AGCCTTTGCT TTCTTATCTA AAAAAAAAAA AAAAAAAATG AAGGAAGGGG TATTAAAAGG   5904
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TATTGTGCAC TTACTATGTG GTACTGTGCT ATAGAGGCTT TAACATTTAT AAAAACACTG   6024
TGAAAGTTGC TTCAGATGAA TATAGGTAGT AGAACGGCAG AACTAGTATT CAAAGCCAGG   6084
TCTGATGAAT CCAAAAACAA ACACCCATTA CTCCCATTTT CTGGGACATA CTTACTCTAC   6144
CCAGATGCTC TGGGCTTTGT AATGCCTATG TAAATAACAT AGTTTTATGT TTGGTTATTT   6204
TCCTATGTAA TGTCTACTTA TATATCTGTA TCTATCTCTT GCTTTGTTTC CAAAGGTAAA   6264
CTATGTGTCT AAATGTGGGC AAAAAATAAC ACACTATTCC AAATTACTGT TCAAATTCCT   6324
TTAAGTCAGT GATAATTATT TGTTTTGACA TTAATCATGA AGTTCCCTGT GGGTACTAGG   6384
TAAACCTTTA ATAGAATGTT AATGTTTGTA TTCATTATAA GAATTTTTGG CTGTTACTTA   6444
TTTACAACAA TATTTCACTC TAATTAGACA TTTACTAAAC TTTCTCTTGA AAACAATGCC   6504
CAAAAAAGAA CATTAGAAGA CACGTAAGCT CAGTTGGTCT CTGCCACTAA GACCAGCCAA   6564
CAGAAGCTTG ATTTTATTCA AACTTTGCAT TTTAGCATAT TTTATCTTGG AAAATTCAAT   6624
TGTGTTGGTT TTTTGTTTTT GTTTGTATTG AATAGACTCT CAGAAATCCA ATTGTTGAGT   6684
AAATCTTCTG GGTTTTCTAA CCTTTCTTTA GAT GTT ACC CTG TGT GAG GAG GCA    6738
                                 Asp Val Thr Leu Cys Glu Glu Ala
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TTC TTC AGG TTT GCT GTT CCT ACA AAG TTT ACG CCT AAC TGG CTT AGT      6786
Phe Phe Arg Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser
185                 190                 195                 200

GTC TTG GTA GAC AAT TTG CCT GGC ACC AAA GTA AAC GCA GAG AGT GTA      6834
Val Leu Val Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val
                205                 210                 215

GAG AGG ATA AAA CGG CAA CAC AGC TCA CAA GAA CAG ACT TTC CAG CTG      6882
Glu Arg Ile Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu
            220                 225                 230

CTG AAG TTA TGG AAA CAT CAA AAC AAA GAC CAA GAT ATA GTC AAG AAG      6930
Leu Lys Leu Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys
        235                 240                 245

ATC ATC CAA GGTAATTACA TTCCAAAATA CGTCTTTGTA CGATTTTGTA              6979
Ile Ile Gln
    250

GTATCATCTC TCTCTCTGAG TTGAACACAA GGCCTCCAGC CACATTCTTG GTCAAACTTA    7039

CATTTTCCCT TTCTTGAATC TTAACCAGCT AAGGCTACTC TCGATGCATT ACTGCTAAAG    7099

CTACCACTCA GAATCTCTCA AAAACTCATC TTCTCACAGA TAACACCTCA AAGCTTGATT    7159

TTCTCTCCTT TCACACTGAA ATCAAATCTT GCCCATAGGC AAAGGGCAGT GTCAAGTTTG    7219

CCACTGAGAT GAAATTAGGA GAGTCCAAAC TGTAGAATTC ACGTTGTGTG TTATTACTTT    7279

CACGAATGTC TGTATTATTA ACTAAAGTAT ATATTGGCAA CTAAGAAGCA AAGTGATATA    7339

AACATGATGA CAAATTAGGC CAGGCATGGT GGCTTACTCC TATAATCCCA ACATTTTGGG    7399

GGGCCAAGGT AGGCAGATCA CTTGAGGTCA GGATTTCAAG ACCAGCCTGA CCAACATGGT    7459

GAAACCTTGT CTCTACTAAA AATACAAAAA TTAGCTGGGC ATGGTAGCAG GCACTTCTAG    7519

TACCAGCTAC TCAGGGCTGA GGCAGGAGAA TCGCTTGAAC CCAGGAGATG GAGGTTGCAG    7579

TGAGCTGAGA TTGTACCACT GCACTCCAGT CTGGGCAACA GAGCAAGATT TCATCACACA    7639

CACACACACA CACACACACA CACACATTAG AAATGTGTAC TTGGCTTTGT TACCTATGGT    7699

ATTAGTGCAT CTATTGCATG GAACTTCCAA GCTACTCTGG TTGTGTTAAG CTCTTCATTG    7759

GGTACAGGTC ACTAGTATTA AGTTCAGGTT ATTCGGATGC ATTCCACGGT AGTGATGACA    7819

ATTCATCAGG CTAGTGTGTG TGTTCACCTT GTCACTCCCA CCACTAGACT AATCTCAGAC    7879

CTTCACTCAA AGACACATTA CACTAAAGAT GATTTGCTTT TTTGTGTTTA ATCAAGCAAT    7939

GGTATAAACC AGCTTGACTC TCCCCAAACA GTTTTTCGTA CTACAAAGAA GTTTATGAAG    7999

CAGAGAAATG TGAATTGATA TATATATGAG ATTCTAACCC AGTTCCAGCA TTGTTTCATT    8059

GTGTAATTGA AATCATAGAC AAGCCATTTT AGCCTTTGCT TTCTTATCTA AAAAAAAAAA    8119

AAAAAAAATG AAGGAAGGGG TATTAAAAGG AGTGATCAAA TTTTAACATT CTCTTTAATT    8179

AATTCATTTT TAATTTTACT TTTTTTCATT TATTGTGCAC TTACTATGTG GTACTGTGCT    8239

ATAGAGGCTT TAACATTTAT AAAAACACTG TGAAAGTTGC TTCAGATGAA TATAGGTAGT    8299

AGAACGGCAG AACTAGTATT CAAAGCCAGG TCTGATGAAT CCAAAAACAA ACACCCATTA    8359

CTCCCATTTT CTGGGACATA CTTACTCTAC CCAGATGCTC TGGGCTTTGT AATGCCTATG    8419
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TAAATAACAT AGTTTTATGT TTGGTTATTT TCCTATGTAA TGTCTACTTA TATATCTGTA 8479

TCTATCTCTT GCTTTGTTTC CAAAGGTAAA CTATGTGTCT AAATGTGGGC AAAAAATAAC 8539

ACACTATTCC AAATTACTGT TCAAATTCCT TTAAGTCAGT GATAATTATT TGTTTTGACA 8599

TTAATCATGA AGTTCCCTGT GGGTACTAGG TAAACCTTTA ATAGAATGTT AATGTTTGTA 8659

TTCATTATAA GAATTTTTGG CTGTTACTTA TTTACAACAA TATTTCACTC TAATTAGACA 8719

TTTACTAAAC TTTCTCTTGA AAACAATGCC CAAAAAAGAA CATTAGAAGA CACGTAAGCT 8779

CAGTTGGTCT CTGCCACTAA GACCAGCCAA CAGAAGCTTG ATTTTATTCA AACTTTGCAT 8839

TTTAGCATAT TTTATCTTGG AAAATTCAAT TGTGTTGGTT TTTTGTTTTT GTTTGTATTG 8899

AATAGACTCT CAGAAATCCA ATTGTTGAGT AAATCTTCTG GGTTTTCTAA CCTTTCTTTA 8959

GAT ATT GAC CTC TGT GAA AAC AGC GTG CAG CGG CAC ATT GGA CAT GCT 9007
Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
255 260 265

AAC CTC ACC TTC GAG CAG CTT CGT AGC TTG ATG GAA AGC TTA CCG GGA 9055
Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
270 275 280

AAG AAA GTG GGA GCA GAA GAC ATT GAA AAA ACA ATA AAG GCA TGC AAA 9103
Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
285 290 295

CCC AGT GAC CAG ATC CTG AAG CTG CTC AGT TTG TGG CGA ATA AAA AAT 9151
Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
300 305 310 315

GGC GAC CAA GAC ACC TTG AAG GGC CTA ATG CAC GCA CTA AAG CAC TCA 9199
Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
320 325 330

AAG ACG TAC CAC TTT CCC AAA ACT GTC ACT CAG AGT CTA AAG AAG ACC 9247
Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
335 340 345

ATC AGG TTC CTT CAC AGC TTC ACA ATG TAC AAA TTG TAT CAG AAG TTA 9295
Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
350 355 360

TTT TTA GAA ATG ATA GGT AAC CAG GTC CAA TCA GTA AAA ATA AGC TGC 9343
Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys
365 370 375

TTA TAACTGGAAA TGGCCATTGA GCTGTTTCCT CACAATTGGC GAGATCCCAT 9396
Leu
380

GGATGAGTAA ACTGTTTCTC AGGCACTTGA GGCTTTCAGT GATATCTTTC TCATTACCAG 9456

TGACTAATTT TGCCACAGGG TACTAAAAGA AACTATGATG TGGAGAAAGG ACTAACATCT 9516

CCTCCAATAA ACCCCAAATG GTTAATCCAA CTGTCAGATC TGGATCGTTA TCTACTGACT 9576

ATATTTTCCC TTATTACTGC TTGCAGTAAT TCAACTGGAA ATTAAAAAAA AAAAACTAGA 9636

CTCCACTGGG CCTTACTAAA TATGGGAATG TCTAACTTAA ATAGCTTTGG GATTCCAGCT 9696

ATGCTAGAGG CTTTTATTAG AAAGCCATAT TTTTTTCTGT AAAAGTTACT AATATATCTG 9756

TAACACTATT ACAGTATTGC TATTTATATT CATTCAGATA TAAGATTTGG ACATATTATC 9816

ATCCTATAAA GAAACGGTAT GACTTAATTT TAGAAAGAAA ATTATATTCT GTTTATTATG 9876

ACAAATGAAA GAGAAAATAT ATATTTTTAA TGGAAAGTTT GTAGCATTTT TCTAATAGGT 9936

ACTGCCATAT TTTTCTGTGT GGAGTATTTT TATAATTTTA TCTGTATAAG CTGTAATATC 9996

ATTTTATAGA AAATGCATTA TTTAGTCAAT TGTTTAATGT TGGAAAACAT ATGAAATATA 10056

AATTATCTGA ATATTAGATG CTCTGAGAAA TTGAATGTAC CTTATTTAAA AGATTTTATG 10116

GTTTTATAAC TATATAAATG ACATTATTAA AGTTTTCAAA TTATTTTTTA TTGCTTTCTC 10176

TGTTGCTTTT ATTT 10190

(2) INFORMATION FOR SEQ ID NO:106:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 391 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

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Phe Leu Asp Ile Ser Ile Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro
-11 -10                  -5                   1               5

Lys Tyr Leu His Tyr Asp Glu Glu Thr Ser His Gln Leu Leu Cys Asp
                 10                  15                  20

Lys Cys Pro Pro Gly Thr Tyr Leu Lys Gln His Cys Thr Ala Lys Trp
             25                  30                  35

Lys Thr Val Cys Ala Pro Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp
         40                  45                  50

His Thr Ser Asp Glu Cys Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu
     55                  60                  65

Gln Tyr Val Lys Gln Glu Cys Asn Arg Thr His Asn Arg Val Cys Glu
 70                  75                  80                  85

Cys Lys Glu Gly Arg Tyr Leu Glu Ile Glu Phe Cys Leu Lys His Arg
                 90                  95                 100

Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala Gly Thr Pro Glu Arg
            105                 110                 115

Asn Thr Val Cys Lys Arg Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr
        120                 125                 130

Ser Ser Lys Ala Pro Cys Arg Lys His Thr Asn Cys Ser Val Phe Gly
    135                 140                 145

Leu Leu Leu Thr Gln Lys Gly Asn Ala Thr His Asp Asn Ile Cys Ser
150                 155                 160                 165

Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile Asp Val Thr Leu Cys
                170                 175                 180

Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr Lys Phe Thr Pro Asn
            185                 190                 195

Trp Leu Ser Val Leu Val Asp Asn Leu Pro Gly Thr Lys Val Asn Ala
        200                 205                 210
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Glu Ser Val Glu Arg Ile Lys Arg Gln His Ser Ser Gln Glu Gln Thr
 215                 220                 225

Phe Gln Leu Leu Lys Leu Trp Lys His Gln Asn Lys Asp Gln Asp Ile
230                 235                 240                 245

Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys Glu Asn Ser Val Gln
                250                 255                 260

Arg His Ile Gly His Ala Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu
            265                 270                 275

Met Glu Ser Leu Pro Gly Lys Lys Val Gly Ala Glu Asp Ile Glu Lys
        280                 285                 290

Thr Ile Lys Ala Cys Lys Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser
    295                 300                 305

Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu Lys Gly Leu Met
310                 315                 320                 325

His Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro Lys Thr Val Thr
                330                 335                 340

Gln Ser Leu Lys Lys Thr Ile Arg Phe Leu His Ser Phe Thr Met Tyr
            345                 350                 355

Lys Leu Tyr Gln Lys Leu Phe Leu Glu Met Ile Gly Asn Gln Val Gln
        360                 365                 370

Ser Val Lys Ile Ser Cys Leu
    375                 380
```

(2) INFORMATION FOR SEQ ID NO:107:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..20
(D) OTHER INFORMATION: /note= "synthetic DNA (primer 2F)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

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CARGARCARA CNTTYCARYT                                                  20
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(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ix) FEATURE:
(A) NAME/KEY: -
(B) LOCATION: 1..21
(D) OTHER INFORMATION: /note= "synthetic DNA (primer 3R)"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

YTTRTACATN GTRAANSWRT G

21